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CHRONIC DACRYOCYSTITIS

ITS CAUSATION AND TREATMENT

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With an auspicious and a drooping eye.—Hamlet, Act 1, Scene 2.

The present material supplements the cases already referred to in a paper [1] on external dacryocystorhinostomy read before the Ophthalmological Society of the United Kingdom in 1932, which dealt with the period from 1929 to 1931.

During the years 1932 to 1939 inclusive, 1,073 patients were seen in the ophthalmic clinic of the Royal Infirmary, Edinburgh, under my charge, whose complaint was watering of one or both eyes. This number represents 2.7 per cent of the total number of new patients attending during these years. Of these, 548, or almost exactly 50 per cent, were adults with dacryocystitis. Patients appearing for the first time with acute dacryocystitis were included in the group with watering of the eyes, as they gave that history.

Fifty cases of congenital dacryocystitis were collected in two and a half years. This is equal to about 2 cases of the congenital form for every 7 of the adult form.

CAUSATION

The explanations offered in current textbooks of the cause of dacryocystitis are disappointing. In most cases it is stated that the disease is due to obstruction of the nasolacrimal passage, and this obstruction is commonly attributed to intranasal disease. In a certain number of cases the condition is attributed to disease of the neighboring bones, to injury or to some other more or less accidental condition. As regards the latter cases, the explanations given are generally acceptable; as regards the former and much larger group, the suggested cause, stenosis of the nasolacrimal canal following nasal disease, cannot be regarded as satisfactory.

In considering the causation it is necessary to direct attention toward the main features of the disease.

1. Traquair, H. M.: External Dacry-Cysto-Rhinostomy, Tr. Ophth. Soc. U. Kingdom **52**:149, 1932.

Age Incidence.—It is impossible to estimate with any degree of accuracy the age of onset of the disease. In this series the average age at the time of operation was 50 years for male and 49 years for female patients. The youngest patient was a girl aged 13, and the oldest a woman aged 80. As the disease was certainly present for several years before operation, the average age of onset may be regarded as somewhere near 40 years.

Sex Incidence.—Seventeen per cent of the patients were males, and 83 per cent females. While the sex incidence is frequently mentioned in textbooks, little serious attention appears to have been paid to it in connection with the etiology. There is no evidence that dacryocystitis in its usual form is associated with any condition which is commoner in females than in males.

It is interesting to note that the incidence of the congenital condition in infants is equal for the two sexes. Of the 50 patients in the cases collected, 26 were boys, and 24, girls.

Social Incidence.—Few cases were met with in private practice, and the patients in the majority of those encountered were of the same social class as the hospital patients. Dacryocystitis is in this respect unlike disease of the nasal sinuses for example.

Here again the congenital form differs, in that the social predilection is not so pronounced.

Geographic Incidence.—From inquiries made in different countries I have obtained the impression that the predominance of females and the social predilection are not so pronounced in other places as in Edinburgh and the surrounding district. It seems probable also that the number of cases of this condition associated with disease of the neighboring parts, e. g., lupus or trachoma, is greater in some countries or places than in others.

I am unaware of any special features in connection with occupational or racial incidence, but no doubt much interesting information could be obtained if these aspects were examined.

Influence of Local Disease or Injury.—In this series of cases disease in the neighboring parts was extremely rare. The sex predilection alone appears to dispose of the idea that the disease originates from the nose. There is no evidence to show that any nasal disease exists which is five times as common in females as in males. During the years 1938 and 1939 only 43 per cent of the patients in the otolaryngologic department suffering from intranasal conditions of all kinds were females. With no condition was there a definite preponderance of females. Lupus of the nose was present in 2 cases; 1 of the patients was a male, and 1 was a female. In 2 cases it was associated with local injury. I am informed by

a dermatologist that the incidence of lupus of the face, and proportionally that of lupus of the inside of the nose, is two to three times greater for women than for men. Dacryocystitis appears to be more common in cases of lupus of the nose in women than would appear from the small number who apply to the ophthalmic clinic. The reason seems to be that the disease of the nose and face as a rule completely overshadows the lacrimal trouble. At the same time, it does not appear to be as common as might be expected if the nasal lupus had any strong influence in determining the condition of the lacrimal sac. In only 1 case (apart from the 2 cases of lupus) was any obvious intranasal pathologic condition present. This was one in which a few small polypi in the middle meatus of a male patient were discovered and removed during the operation. In addition, I have observed at various times 3 cases which do not come within the scope of these figures—1 a case of lupus in a male, the second a case of acute inflammation of the antrum in a male [2] and the third a case of cancer of the maxilla in a female. The much smaller number of private cases included 1 case of injury and 1 case of lupus, which indicates that the incidence of dacryocystitis of the type connected with local disease is larger in private practice.

In no case was a preliminary rhinologic examination undertaken, and nothing was found during the operation or later to indicate that the treatment would have required modification or that the results would have been different had such an examination been made.

Of all the patients who applied in the first place to the rhinologic department on account of nasal trouble, only 1 was referred from that department to the ophthalmic department on account of dacryocystitis.[3] This would seem to indicate at least that such conditions as deviated septum, swollen turbinates and the common chronic intranasal sinal or antral inflammations are not frequently associated with dacryocystitis. Both nasal catarrh and conjunctivitis are more common in children than in adults, and coryza is common in children of all classes, but dacryocystitis is rare in children of school age. Thus both the social incidence and the age incidence are against a causal relationship with coryza. None of the patients gave any history of chronic nasal trouble.

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2. Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 3. Bailliart, P.; Coutela, C.; Redslov, E., and Velter, E.: Traité d'ophtalmologie, Paris, Masson & Cie, 1939, vol. 4.

3. This patient was a male who was in the rhinologic department on account of osteomyelitis affecting the right frontal and zygomatic bones and the maxilla and severe inflammation of the antrum. Dacryocystitis developed on the same side. The patient died of cavernous sinus thrombosis. This is the only case of dacryocystitis referred from the rhinologic department during the years mentioned. The condition belongs to the secondary dacryocystitis group.

In the incipient stage of the disease there is epiphora, and the nasolacrimal duct is patent and may be syringed through with little or no difficulty. This patency may persist, and in many cases it was found that the patient was accustomed to express the contents of the sac downward into the nose. That this can often be done is familiar to all ophthalmic surgeons. Obstruction develops at the lower end of the sac, at the entrance to the lacrimal canal, and is not a primary feature but may be regarded as a result of the disease.

Averbakh and Ivanova [4] had the nose examined in 392 of 1,200 cases. In 33 per cent this organ was normal, and in the others there were nasal conditions such as may occur without dacryocystitis and without influence on the operation. Nothing of importance was disclosed in any of the cases.

If these data are studied it is apparent that there are two kinds of dacryocystitis. The first and most common is characterized by pronounced sex and social predilections and by the absence of any obvious causal factor. Following the terminology used for glaucoma, this may be called primary dacryocystitis. The second type, which has a much smaller incidence, is associated with contributory factors, such as local disease of various kinds or local injury, and may be called secondary dacryocystitis. Owing to the small incidence (less than 1 per cent of the cases under review) it is not possible to obtain conclusive data as to the sex and social incidence, but there seems no doubt that in these respects it does not present the prominent features characteristic of the first type. As might be expected, its incidence among males is greater, and it is relatively more common in private practice.

It follows from this pronounced tendency for females to be affected that if intranasal disease and dacryocystitis are associated in a female it is still open to question whether the two conditions are not merely coincidental. In the case of a male a causal relation is much more strongly indicated. In either case the presence of other patients in the family suggests that the nasal condition is not really the cause.

In some cases epiphora without obvious cause is cured by syringing through the nasolacrimal canal once or twice, although there is not necessarily any obstruction. In others the patients return months or years afterward with manifest dacryocystitis. Epiphora without obvious cause occurs largely in females, which suggests the possibility that it may represent an abortive form of primary dacryocystitis.

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4. Averbakh, I., and Ivanova (Mme.): Douze cents opérations de dacryocystorhinostomie plastique, Ann. d'ocul. **172**:913, 1935.

If obstruction of the nasolacrimal passage were the most important causal factor one would expect that the use of a probe to clear the canal would result in more cures. In my experience this form of treatment benefits the patient occasionally in an early stage and at best merely postpones the necessity of more thorough measures.

The cure of congenital dacryocystitis, which is frequently purulent, by one probing seems to show that at that age the sac, though easily infected, has a strong natural power of recovery and that the canal, though covered at its lower end by a membrane, does not tend to become progressively stenosed. It is otherwise with the adult form, which often exists together with a patent or only partly stenosed canal and in which the sac is more resistant to infection but shows no tendency to recovery and obstinately withstands probing and syringing. If drainage is adequate the adult sac resists infection both from above and from below. In cases of acute or chronic conjunctivitis enormous numbers of pathogenic organisms must pass through the sac, but infection does not take place. In cases of nasal disease it might be expected that organisms would not travel upward against the stream, but they must often be forced upward by violent blowing of the nose. Persons who can whistle through their canaliculi do not seem to be especially liable to dacryocystitis. It seems probable that the rare occurrences of lupus, and tuberculosis or other infection of the sac from neighboring parts is due to direct extension of the disease rather than to influx of infective organisms either from above or from below. It would appear that the sac is resistant to infective organisms in a much higher degree than the conjunctiva and that it becomes infected only if stasis, partial or complete, of its contents is present. In many cases, even in the presence of complete stasis infection does not take place.

Chronic dacryocystitis is often referred to as an "infection" of the sac. There is no evidence pointing to an infectious origin, although a sac already affected by the disease may become infected.

These considerations suggest that primary dacryocystitis develops somewhat as follows: A swelling of the mucous membrane occurs, involving the nasolacrimal canal or both the sac and the canal. This leads to stasis of the contents of the sac, and a vicious circle arises, leading finally to blocking of the canal and distention of the sac, with or without subsequent infection of its contents. Obstruction of the duct is not a necessary preliminary.

What can be the cause of the primary form? No conclusion which does not take into consideration the sex and social incidence can be regarded as valid. The pronounced sex predilection points strongly toward a hereditary or a familial factor, especially as there is no local

contributory cause which is five times as common in women as in men. The social incidence by itself might be regarded as having a nutritional or a hygienic significance, but such an explanation is excluded by the sex predilection, and the social incidence may be regarded as affording additional support to the view that heredity is important. The hereditary and familial factors in dacryocystitis have been noted for many years. Mackenzie [5] noticed 2 sisters with the disease, and no doubt many similar cases had been observed before his time. More recently increasing attention has been paid to this factor; it was referred to by Haab,[6] Nieden,[7] Schnyder,[8] Vogt,[9] Waardenburg [10] and others. Except by Haab and Nieden, who attached great importance to it, the influence of heredity has not usually been regarded as of serious significance in the causation of the disease.

In the present series, inquiries as to family history were made only during the last four or five years, and during that period definite evidence of a hereditary factor was found in 11 per cent of the cases in which the patients were admitted for operation. Such an element probably exists in a larger proportion, as many of the patients do not know much about their parents' or their relatives' ocular conditions, and, as with other hereditary ocular diseases, many patients who do not report anything significant in the family history probably have dacryocystitis which is hereditary in origin. On the other hand, when the hereditary element is prominent the different members of the family are often well aware of it. Dr. Bruce Hamilton, of Hobart, Tasmania, who is interested in hereditary diseases of the eye, sent me privately a number of pedigrees illustrating heredity in cases of dacryocystitis which he had observed. In his cases the uncorrected percentages for adult sex incidence were 79 for women and 21 for men; for infant sex incidence, 57 for girls and 43 for boys. The most striking example of heredity which has come under my observation occurred in a private patient's family, and I was

5. Mackenzie, W.: A Practical Treatise on the Diseases of the Eye, ed. 4, London, Longman [and others], 1854.

6. Haab, O.: Atlas of the External Diseases of the Eye, ed. 2, Philadelphia, W. B. Saunders Company, 1903.

7. Nieden, A.: Ueber das Vorkommen und die Erblichkeit von Erkrankungen der Thränenableitungswege, Centralbl. f. prakt. Augenh. **7**:301-305, 1883.

8. Schnyder, W. F.: Ueber familiäres Vorkommen resp. die Vererbung von Erkrankungen der Tränenwege, Ztschr. f. Augenh. **44**:257, 1920.

9. Vogt, A.: Hereditäre Dakryocystoblennorrhoe, Klin. Monatsbl. f. Augenh. **85**:281, 1930.

10. Waardenburg, P. J.: Das menschliche Auge und seine Erbanlagen, The Hague, Martinus Nijhoff, 1932, p. 82.

11 and 12. References deleted by the author.

therefore able to obtain more information than from the hospital cases. In this case 1 man who had dacryocystitis had sixteen descendants, among whom were 12 with dacryocystitis, 4 males and 8 females (fig. 1). The disease was well known in the family as a hereditary manifestation,

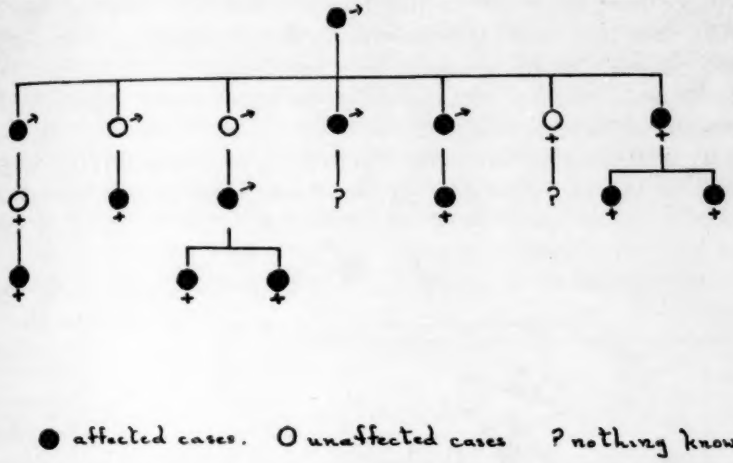

Fig. 1.—Pedigree showing descent through both affected and unaffected males to females.

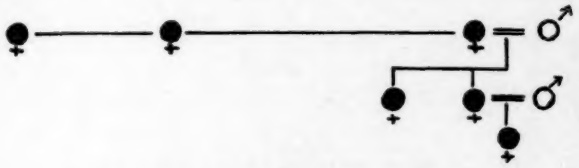

Fig. 2.—Pedigree showing all affected females.

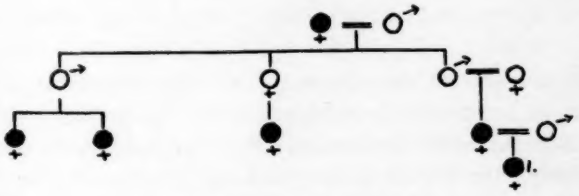

Fig. 3.—Pedigree showing all affected females, the youngest (*1*) being an infant.

but I was unfortunately unable to obtain a complete family tree, so that the proportion of 12 to 16 is probably incorrect. In figure 3 are represented 5 female patients descended from 1 female affected through unaffected males and females; the youngest patient was an infant.

The congenital form may be present in several children in the same family; its inheritance from parents who have the adult form is interesting (figs. 3 and 4), but as the two forms show definite clinical differences the significance of this hereditary factor is not clear. Nieden found a definite predominance of inheritance from mother to children over inheritance from father to children and of inheritance from mother to daughter over inheritance from mother to son. Inheritance from father to daughter and that from father to son were equal.

As regards primary dacryocystitis, heredity would appear to be the most important cause.

If these views are correct the cause of dacryocystitis is stasis of the contents of the sac, dependent in the primary form on a hereditary

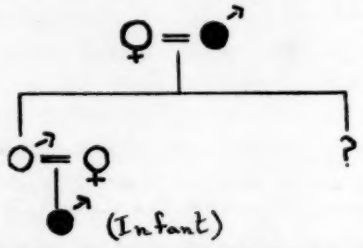

Fig. 4.—Congenital form of the condition in a male descended from a male who had the condition in adult life. (By permission of Dr. Bruce Hamilton.)

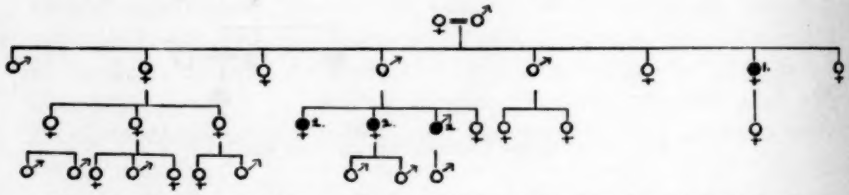

Fig. 5.—*1*, dacryocystitis at the age of 16. *2*, 3 affected newborn infants.

tendency to progressive stenosis of the lacrimal canal and in the secondary form to an accidental obstruction from disease or injury of adjoining parts. With the primary form there does not seem to be any evidence to show whether the disease commences in the sac or in the canal. The fact that in many of the cases the condition is not associated with pathogenic bacteria suggests that the disease may originate in the canal. No evidence has been recorded as to whether infants who have been cured of congenital dacryocystitis have the adult form in later years or themselves affect infants or children unaffected at birth who become affected in adult life. However, it should not be impossible to obtain some information on this question.

Bacteriologic Picture.—A bacteriologic examination was made of the conjunctival sac in 251 cases in which Toti's operation was subsequently performed, and the conjunctival sac was reexamined after the operation in 95 cases. Two hundred and twenty-five cataractous eyes formed a control. The micro-organisms present were arranged in this order: pneumococci; streptococci; Staphylococcus aureus; Staphylococcus albus, and miscellaneous organisms. Cultures which showed no growth were placed in a final group. When a culture showed pneumococci it was classed in the pneumococcic group even though organisms of the following four kinds were present; if streptococci were present the culture was included in the streptococcic group even though organisms of the following three groups were present, and so on. The group of "other organisms" was composed mostly of diphtheroids and a few coliform bacilli; it contained none of the previous four groups. The results were as follows:

	Before Operation		After Operation		Controls	
Pneumococci	24%	32%	8%	11%	1%	6%
Streptococci	8%		3%		5%	
Staph. aureus	6%	68%	2%	89%	3%	94%
Staph. albus	26%		36%		40%	
Other organisms	24%		27%		35%	
No growth	12%		24%		16%	

If these figures are arranged in two groups, the first including pneumococci and streptococci and designated as the virulent group and the second including the staphylococci, other organisms and cultures with no growth and designated as the less virulent group, it will be seen that pneumococci and streptococci together are five times as numerous in the dacryocystitic conjunctiva as in the normal conjunctiva and that this difference is mainly due to the pneumococcus, which was found in 24 per cent of the patients as against only 1 per cent of the controls. The incidence of cultures with no growth was about equal, 12 per cent and 16 per cent respectively. These results are on the whole in agreement with those found by Continental observers.[1]

The effect of the operation was to reduce the virulent group from 32 per cent to 11 per cent and to increase the less virulent group from 68 per cent to 89 per cent; in other words, to bring the figures close to those noted for the controls, which were 6 per cent and 94 per cent respectively. If the acutely involved eyes are taken alone the virulent group is relatively slightly larger, being 37 per cent as against 32 per cent in all the cases. Thus the inclusion of cases of acute involvement has little influence on the distribution of bacteria in the conjunctival sac in all cases of dacryocystitis. After operation the figures were 11 per cent and 89 per cent, showing that the same result was obtained for cases of

acute involvement only as for the total series. Several operations for cataract were done after the Toti operation, without any reaction in the eye.

TREATMENT

Congenital Form.—This is often mistaken for conjunctivitis or even for ophthalmia neonatorum. The puncta should be well exposed, and pressure should be made on the sac with the rounded end of a glass rod about 5 mm. in diameter to ascertain the presence of mucopus in the sac.

As is well known, this form of dacryocystitis can usually be cured by one passage of a probe. Ethyl chloride anesthesia is sufficient. The upper punctum is opened by a dilator, which should have a fine but rounded point and a gradual slope. The probe should not be too fine and should be passed gently through the canaliculus and the sac. Great care should be taken to avoid the formation of false passages. When the probe has been passed into the canal it is important to push it down smartly until it impinges on the floor of the nose, as the obstruction frequently consists of a fine membrane covering the lower orifice of the canal. The passage may then be gently syringed with saline solution, with avoidance of the use of force. The baby should be turned on its face so that the fluid runs out of the nose.

Should a false passage have been made, fluid may escape into the tissues of the face. This causes some swelling but does no harm. If the syringe is used, suspicion should be aroused if the fluid disappears but does not appear at the nose.

Adult Form.—In the early stages epiphora alone may be present, and the question arises whether this epiphora is an indication of dacryocystitis in its earliest stage. If the patient is a woman and there is a family history of watering eyes the existence or the development of dacryocystitis is extremely probable even if there is no regurgitation and the lacrimal passage proves to be patent and easily washed through. While syringing may occasionally retard the development of the disease in such circumstances, it rarely prevents it and is nearly always merely a waste of time. If regurgitation of mucus or of mucopurulent matter can be produced by pressure on the sac it is necessary either to excise or to destroy the sac or to drain it into the nose. Excision of the sac rarely secures freedom from watering. It is said that even if the watering does not cease at first it will stop after a year or so, but this has certainly not been my experience. The conjunctivitis ceases, and, although the patient may not complain much of watering, the wet state of the eye remains evident.

If a really satisfactory result is desired, that is an eye without pathologic watering, a drainage operation is essential. Of the various

forms of operation which have from time to time been advocated, a modification of Toti's external dacryocystorhinostomy is both simple and efficacious and has been used in the cases under review. A method of doing this operation was described in the paper already referred to. In the present series the technic has been altered by omitting the trephine and the burr and by cutting a flap of nasal mucosa which is sutured to the sac wall. Removal of the anterior end of the middle turbinated body is unnecessary.

Local anesthesia is adequate except for very young children.

Two solutions are used. For surface anesthesia of the conjunctiva:

Cocaine hydrochloride 10%	10	cc.
Epinephrine hydrochloride 1:1,000	3	cc.
Distilled water to	30	cc.

For infiltration:

Epinephrine hydrochloride 1:1,000	1.5	
Procaine	1.5	
Potassium sulfate	0.4	
Distilled water to	100.0	
Mitte	15	cc.

Three or 4 drops of the cocaine solution is applied to the conjunctival sac at intervals of two or three minutes. The middle meatus of the nose is sprayed with a drop or two of the same solution, and after about a minute a small cotton wool swab to which a thread is attached, soaked in the solution, is pushed up to the anterior part of the middle meatus. A syringe containing about 5 cc. of the procaine solution with a fine needle (British gage 27) 2 inches (5 cm.) long is used. The needle should be entered in the midline of the orbit, about 1 inch (2.5 cm.) below the lower orbital margin, and directed backward and slightly upward. As soon as the point of the needle is beneath the skin the injection should commence, and it should be made very slowly as the needle is pushed onward. The point of the needle should strike the periosteum at or close to the infraorbital nerve as it emerges from its foramen. The region of the foramen should be well infiltrated, and the needle should then be withdrawn until the point is just beneath the skin. The needle should next be directed inward and upward toward the sac region and pushed slowly onward close to the periosteal level, the solution being injected in such a way that the point of the needle continually penetrates tissues already infiltrated. The injection is continued until the skin below the internal palpebral ligament is seen to rise slightly. The second injection is made on the inner side of the orbit, just below the trochlea, the needle being pushed slowly in the same way about ½ inch (1.2 cm.) backward along the orbital wall, close to the periosteum. A drop or

two of the anesthetic may be injected in the neighborhood of each canaliculus. The two injections should use about 4 cc. of the solution. The patency of the canaliculi is now established, if this has not been done beforehand, and a probe may be passed through each canaliculus into the sac, which should then be washed out.

The incision commences immediately below the internal palpebral ligament, at a point about 2 or 3 mm. from the inner canthus. The

Fig. 6.—Position of punctures for local anesthesia and line of incision.

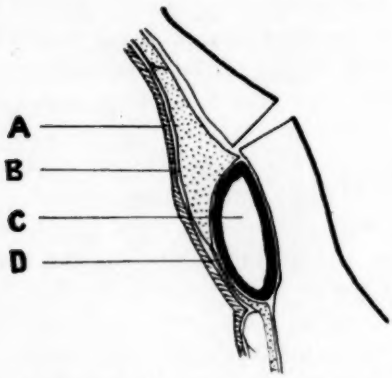

Fig. 7.—Diagrammatic representation of a cross section through the operative area. The incision is shown passing down to a point immediately in front of the anterior lacrimal crest. *A*, mucous membrane of the nose; *B*, maxilla; *C*, lacrimal sac; *D*, lacrimal bone.

point of the knife is directed backward and inward, and the knife is passed directly down to the bone, which it should strike at, or immediately in front of, the upper end of the anterior lacrimal crest. The incision is made downward, curving slightly outward along the line of the crest, and should be about 2.5 cm. long. Retractors are inserted

and held by an assistant, who, by exercising suitable pressure, can easily check any bleeding which may occur. Severe hemorrhage is uncommon if the incision is not placed too far forward. It is unnecessary to divide the internal palpebral ligament, and nothing is gained by extending the incision upward. The edge of the anterior lacrimal crest is now defined and the periosteum divided along it so that the sac can be pushed outward to expose the surface of the maxillary bone, which forms the anterior half of the lacrimal fossa. The surface of the bone forming the anterior wall of the nasolacrimal canal is cleaned, and the lower end of the anterior lacrimal crest, where it overhangs the opening of the canal, is freely removed with a punch forceps so that the upper part of the nasolacrimal duct is exposed. This exposure should be carried well downward. The sac and the upper part of the duct are then drawn

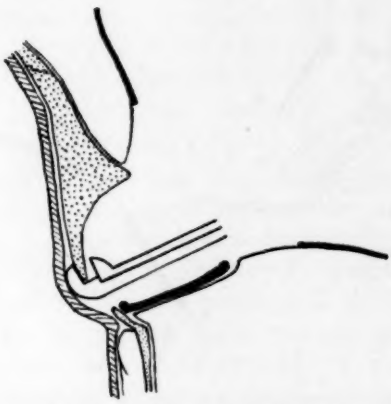

Fig. 8.—The wound has been widely opened and the lacrimal sac retracted out of the fossa. The medial wall of the sac and part of the lacrimal bone have been removed. The punch is inserted to remove the maxilla.

outward so as to expose the posterior part of the lacrimal fossa, formed by the lacrimal bone. The sac is then incised vertically along its anterior surface. The incision should commence 2 or 3 mm. below the entrance of the canaliculi and slightly to the outer side of the midline of the sac. As it is carried downward it is inclined inward so as to leave about 2 mm. of free sac wall on the outer side at the lower end. The inner side of the sac is then removed, only the outer wall (including the inner orifices of the canaliculi) being left. A fine catgut suture is inserted at the upper end of the incision so as to include a little of the adjoining tissue as well as the sac wall. A similar suture is inserted into the margin of the sac below, and the two sutures are clamped and laid aside. As the lower end of the sac lies deeper than the upper, the advantage of leaving a small portion of free sac wall at the lower end

is apparent. The packing is next removed from the nose so as to leave the nasal cavity free. With a small periosteum elevator with a blade 2 mm. wide and 0.5 mm. thick, the terminal 2 mm. being bent to a right angle and the other end being similarly constructed except that the bent portion is 3 mm. long, the lacrimal bone is gently depressed and broken at its lower part. The fragments are picked away, and the end of the periosteum elevator is passed under the edge of the maxilla so as to separate the mucous membrane of the nose from the bone. A small punch forceps of the Kofler pattern is inserted to bite away the maxilla. When one is inserting the punch for the first time, great care should be taken that the mucous membrane is separated from the bone, so that it will not be injured by the end of the punch. If there is any difficulty in access the edge of the maxilla may first be thinned down by a burr. As the hole is extended a larger punch may be used. The

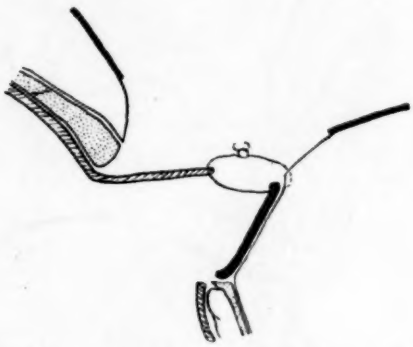

Fig. 9.—The bone has been removed, and the flap of nasal mucosa has been cut and pulled outward. The diagram shows a catgut stitch connecting the edge of the flap to the anterior edge of the wall of the sac.

maxilla is punched away until a hole measuring about 1.75 cm. vertically by 1.25 cm. laterally has been made. The hole should be rectangular and should be extended upward if possible to the level of the canaliculi or until ethmoid cells are encountered. If any bleeding should occur during this process, swabs moistened with the cocaine-epinephrine solution may be packed into the wound. While one is using the punch the edges of the hole in the bone should be made smooth and even, and great care should be taken not to damage the mucous membrane. A rectangular flap of the mucous membrane is cut, corresponding to the margins of the hole. The sutures already in position are passed through the corners of the flap so as to unite them to the anterior edge of the outer wall of the sac. Before tying the catgut sutures it is well to pass a probe through a canaliculus to make sure that the canaliculi open freely into the nose behind the flap. A small pad fixed with adhesive plaster

and kept on for one or two days is sufficient dressing. No packing should be placed in the nose. The patient walks back to bed and remains in bed for that day but is usually able to get up on the second day. On the fourth or the fifth day the stitches are removed and the patient may go home. The canaliculi may be syringed through if desired, but this is not usually necessary.

Complications.—Hemorrhage so troublesome as to prevent completion of the operation and also serious postoperative hemorrhage have been recorded, but in the total of 462 operations performed in this series, together with those in the cases already referred to, no troublesome hemorrhage was experienced during the operation, and in only 3 or 4 cases did postoperative hemorrage occur. In only 2 of these did the hemorrhage persist for several days, and in neither did any serious result ensue.

Other complications occur occasionally in the form of anatomic anomalies, such as variations in the relation of the ethmoid cells or of the middle turbinate to the lacrimal fossa. No complication of this kind was encountered which was sufficiently pronounced to make any difference in the conduct of the operation.

Contraindications.—There are few contraindications. Sometimes the operation is difficult in children, owing to the small size of the parts. The operation is not likely to be successful if the junction of the canaliculi with the sac is cicatrized. If in such circumstances a passage is forced into the nose through the canaliculi it is likely to close again. If owing to previous acute inflammation the sac has been reduced to a fibrous mass with at most a small irregular cavity, success cannot be insured, as it is necessary to have a certain amount of free sac wall around the entrance of the canaliculi. If such conditions are found, excision is safer. If a fistula is present the incision may be carried through it or slightly to one side, according to the state of the tissues. The fistula should be scraped and will heal when drainage is established.

Three hundred and thirty-five external dacryocystorhinostomies were done, and the sac was excised 74 times, making 409 operations on 391 patients. In 5 cases dacryocystorhinostomy was done on both sides, and in 13, on one side, excision being carried out on the other.

Inquiries as to the result were made in all the cases, and 321 replies were received. In 80 per cent of the dacryocystorhinostomized eyes the watering was said to have ceased. Many of the patients wrote letters expressing their great satisfaction. During the last two or three years many of the operations have been performed by the junior staff of the clinic.

In the previous series of cases, before suturing of the mucous membrane flap was employed, 71 per cent of the operations were successful.

Only 35 per cent of the excision operations done during the same period produced completely satisfactory results. In those cases in which excision had been done on one side and dacryocystorhinostomy on the other the difference between the two eyes was striking.

In my experience removal of the palpebral or of the main lacrimal gland or both or injection of alcohol into the gland is unreliable for relief of watering after excision of the sac, though an occasional good result may be obtained.

These figures show the superiority of external dacryocystorhinostomy over excision. They demonstrate also that the former operation gives excellent results even in the hands of relatively inexperienced operators.

CONCLUSIONS

1. There are two forms of chronic dacryocystitis, primary and secondary.

2. The primary form is common and is characterized by a pronounced sex predilection, occurring in women to the extent of 80 per cent or more. Heredity appears to be the most important factor in its causation.

3. The secondary form is rare and occurs approximately equally in the two sexes. It is due to injury or disease of the neighboring parts.

4. The best treatment is a drainage operation, such as external dacryocystorhinostomy.

THE OCULAR FUNDUS IN DIABETES MELLITUS

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Ophthalmologic opinion has been somewhat divided as to whether retinal changes typical of diabetes mellitus are manifestations of the disease itself or are due to alterations of the blood vessels in the retina or to abnormalities of blood pressure caused by the disease. If the latter is true, obviously conditions other than diabetes may cause similar retinal changes. Hence the problem is one of both clinical and theoretic interest.

General opinion favors the view that the ophthalmic changes are secondary to vascular changes. A particularly illuminating discussion is found in a symposium on diabetic retinitis in which Downey,[1] discussing the subject from the point of view of the ophthalmologist, stated that most textbooks deal with diabetic retinitis in a very dogmatic way. In referring to the recent studies by Wagener and Wilder and by Benedict, he brought up the question whether diabetic retinitis as distinct from arteriosclerotic retinitis actually exists. Patients with juvenile diabetes, even of the most severe type, do not have retinitis.

On the other hand, typical retinitis punctata centralis is seen only occasionally in cases of arteriosclerosis with no signs of diabetes. These cases, however, are extremely rare as compared with cases of true diabetic retinitis, and if it is to be assumed that the arteriosclerosis alone is responsible for the retinitis in diabetic persons it is difficult to understand the rarity of the picture in a condition as frequent as arteriosclerosis without diabetes. It would seem that both factors must be operative in the usual case of diabetic retinitis. The whole subject is greatly complicated by the fact that neither diabetes nor diabetic retinitis is a single disease entity, though knowledge of the distinction between the different subgroups is as yet imperfect.

Leopold,[2] speaking from the point of view of the internist, said that the arteriosclerosis of diabetic persons is of the usual senile type and

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1. Downey, J. W., in Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:61-62 (Jan.) 1925.

2. Leopold, E., in Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:61 (Jan.) 1925.

that the retinitis occurs only in elderly and arteriosclerotic persons. Neither hyperglycemia nor hyperacetonemia can cause the retinal lesions. He expressed the belief that in diabetic retinitis the arteriosclerosis is the important element and the diabetes is secondary. Friedenwald [3] discussed the pathologic aspects of diabetic retinitis. Surprisingly little is known about this condition. Perhaps some light may be thrown on the relation between diabetes and arteriosclerosis in the causation of retinal lesions when more is known about arteriosclerosis. At present physicians diagnose arteriosclerosis without questioning whether the larger or the smaller vessels are involved, though variations in the localization of the lesions may result in quite different clinical pictures. The part played by changes in the capillaries in the production of different forms of retinitis has not yet been studied. Clapp [4] stated that the question of the cause of diabetic retinitis had aroused attention as far back as 1870. Nettleship and others of his generation engaged in a lively discussion as to whether diabetic retinitis exists as a separate entity, distinct from nephritic retinitis.

Friedenwald [5] stated that diabetes alone cannot cause the retinal changes, as is shown by the absence of these changes in young diabetic patients. However, the diabetes must play a definite part in the production of these lesions, perhaps through abnormalities of metabolism; otherwise it is not possible to explain the relative rarity of this ophthalmoscopic picture in cases of arteriosclerosis without diabetes. One questions the part which the associated hypertension plays in the production of these lesions, for the similarity of the lesions of arteriosclerosis associated with hypertension approaching the malignant stage and those seen in cases of diabetic retinitis is impressive. Goldbach [6] said: "The lesions in diabetic and advanced arteriosclerotic retinitis are somewhat similar, and it is difficult to say definitely whether the diabetic or the cardiovascular condition is the greater factor as the underlying cause of the retinal changes."

Parker [7] maintained that retinitis occurs late in the disease and usually in patients over 50 years of age. In its typical form diabetic retinitis may be suspected.

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3. Friedenwald, J. S., in Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:61 (Jan.) 1925.

4. Clapp, C. A., in Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:62 (Jan.) 1925.

5. Friedenwald, H., in Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:62 (Jan.) 1925.

6. Goldbach, in Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:62 (Jan.) 1925.

7. Parker, W. R.: Ocular Manifestations of Diabetes, Am. J. Ophth. **8**:284-287 (April) 1925.

Wilder [8] stated that he had rarely if ever encountered a case of retinitis occurring in a diabetic person in which careful ophthalmoscopic study would not reveal evidences of arterial changes. Similar observations, according to him, were made in a large number of cases in the Mayo Clinic, and he expressed the opinion that such sclerosis of the retinal vessels might be sufficient to account for the hemorrhages as well as for the other lesions associated with so-called diabetic retinitis.

Gradle [9] summed up the observations of Wagener and Wilder. The results were striking:

1. Retinitis did not occur in cases of uncomplicated diabetes, even of the severe type. (It was not present in 80 consecutive cases.)

2. Diabetes with retinitis was always complicated by vascular or renal disease, and the diabetes was apt to be mild and chronic.

3. The cause of the retinitis associated with diabetes seemed to lie in the accompanying vascular changes.

He also maintained, according to Ottfried Müller, Weiss, Zeller and others, that in cases of diabetes, hypertonicity and nephritis marked changes are observed microscopically in the capillaries. Vollhard [10] stated that he has never encountered a case of diabetic retinitis in which there were not the other histopathologic changes in the capillaries. In all cases of retinitis in diabetic persons observed by Gradle himself there was more or less retinal sclerosis, and his impression was that the retinitis associated with diabetes is due either to vascular hypertension or to nephritis (in its broadest sense).

The fundus picture in cases of diabetic retinitis, according to Cohen,[11] is frequently difficult or impossible to differentiate from that in cases of renal or arteriosclerotic retinitis, owing to the primary vascular pathologic process common to all. In the presence of diabetic retinitis the retinal vessels frequently show definite pathologic evidence of varying degrees of arteriosclerosis. General hypertension, if present, is apt to aggravate the lesion of the fundus. According to him some clinicians claim that hypertension is a forerunner of arteriosclerosis and that this arteriosclerosis culminates in diabetes.

When diabetic retinitis is complicated by nephritis or arteriosclerosis the retinal picture is not especially significant of either of the two diseases unless that complication is predominant. Cohen concluded that diabetic retinitis is due mainly to disease of the retinal vessels and that

8. Wilder, W. H., in discussion on Gradle.[9]

9. Gradle, H.: Ocular Conditions in Diabetes, Am. J. Ophth. **10**:54-55 (Jan.)1927.

10. Vollhard, in discussion on Gradle.[9]

11. Cohen, M.: The Eye in Diabetes Mellitus, Arch. Ophth. **2**:530-532 (Nov.) 1929.

in some instances diabetes influences the fundus picture in an early stage. He stated that he is inclined to consider diabetic retinitis either as retinal arteriosclerosis associated with diabetes or, if the vascular lesion is severe, as arteriosclerotic retinitis associated with diabetes. Diabetic retinitis, according to him, is frequently difficult or impossible to distinguish from renal and arteriosclerotic retinitis.

Cammidge [12] concluded from his series of 1,000 cases that it is doubtful whether retinitis due to diabetes alone has ever occurred.

Rosenberg [13] expressed the opinion that from the point of view of the oculist it is wise to divide diabetes into two types, the severe diabetes of youth and the mild diabetes of old age. The aged diabetic person frequently has severe arterial disease, and most of the ocular complications are caused not by the diabetes but by the angiosclerosis. The retinitis of diabetes is never found in young persons and is a vascular form of retinitis. However, the form of retinitis with white spots about the macula and the disk is so characteristic that the hyperglycemia, or diabetic metabolism, may be an accompanying etiologic factor. The hemorrhages have nothing to do with diabetes.

Garretón and Camino [14] in their studies ot 137 cases of diabetes, including 32 cases of retinitis, showed that retinitis was mainly associated with hypertension, advanced age (between 45 and 55 years) and diabetes of long standing. The association of renal disease was not significant, but cardioaortic involvement was marked, although it did not parallel the gravity of the diabetes. The retinitis is therefore primarily a phenomenon of hypertension. Gresser [15] in his series of 100 cases found retinopathy associated with sclerosis and hypertensive signs in 38 per cent. In 30 per cent there were signs of retinal vascular sclerosis without other vascular or retinal changes. In 32 per cent there were no alterations in the retinal vessels or tissues.

Garretón and Camino [14] reported that the retinitis of diabetes depends exclusively on the vascular and sclerotic lesions which complicate this disease and is therefore to be found only in cases of old involvement. It has no significance in connection with the severity of the existing diabetes, the process depending on the hypertension accompanying the vascular complications.

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12. Cammidge, P. J.: Proc. Roy. Soc. Med. (Sect. Ophth.) **23**:24-32 (Jan.) 1930.

13. Rosenberg, M.: Ztschr. f. Augenh. **73**:207-213 (Feb.) 1931; abstracted, Am. J. Ophth. **14**:995-996 (Sept.) 1931.

14. Garretón, A., and Camino, C.: Diabetic Retinitis, Arch. de oftal. hispano-am. **32**:185-196 (April) 1932; abstracted, Am. J. Ophth. **15**:875 (Sept.) 1932.

15. Gresser, E. B.: Studies of Retinopathies: Diabetes Mellitus, Am. J. Ophth. **16**:612-619 (July) 1933.

Wagener, Dry and Wilder [16] in their series of 1,052 cases found the retinal lesions occurring mostly in patients over 40 years of age. They were usually associated with hypertension or with other evidence of general vascular disease. In this series 12 per cent of patients were entirely free from vascular diseases. The authors expressed the belief that diabetes injures the finer arterioles or venules, probably the latter. When the patient is afflicted with other disease of the vascular system, particularly hypertension, the lesion characteristic of diabetes is superimposed. Dirion [17] in her summary noted the following points:

1. Diabetic retinitis is not a definite entity.

2. Most of the patients with diabetic retinitis who were studied had arteriosclerosis.

3. The majority of the patients under discussion had hypertension. Arruga [18] in his series of 20,000 cases found that diabetic retinitis is most serious when associated with hemorrhagic glaucoma and that it is the consequence of sclerosis and degeneration of the retinal blood vessels, the amount of blood sugar bearing no relation to its production. Albuminuria is often coexistent, and it is frequently difficult to determine which is the responsible etiologic factor. From a pathologic point of view the lesion consists of obliterating arteritis with fatty degeneration, sclerosis of the vessel walls and hemorrhages.

Bessière [19] expressed the belief that two opposing theories have developed, one that the retinitis of diabetes is independent of any disease of the kidneys and the other that hemorrhages and exudates appear only in diabetic persons who also have albuminuria and hypertension. The retinitis does not develop at any time during the evolution of the diabetes and never appears in young persons, even though other ocular changes may be present. He also stated that the changes come on between the ages of 50 and 60, developing slowly and without definite relation to the degree of glycosuria, the blood sugar content or similar factors. In some instances they occur at the same time that renal changes become evident; in others they develop when albuminuria has been present for a short time, sometimes when there are few or no indications of disease of the kidneys. Patients with diabetic retinitis are usually arteriosclerotic and have been glycosuric for a long time, and in some there is evidence of renal failure.

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16. Wagener, H. P.; Dry, T. J., and Wilder, R. M.: Retinitis in Diabetes, New England J. Med. **211**:1131-1137 (Dec. 20) 1934; abstracted, Am. J. Ophth. **18**:883 (Sept.) 1935.

17. Dirion, J. K.: Diabetic Retinitis, Arch. Ophth. **9**:829-839 (May) 1933.

18. Arruga, H.: Ocular Diabetes, Arch. de oftal. hispano-am. **33**:356-367 (July) 1932; abstracted, Arch. Ophth. **9**:286 (Feb.) 1933.

19. Bessière, E.: Does Diabetic Retinitis Occur in the Absence of Renal Changes? Arch. d'opht. **49**:219-248 (April) 1932; abstracted, Arch. Ophth. **10**: 273-274 (Aug.) 1933.

Waite [20] expressed the opinion that the retinal hemorrhages are due not to diabetes alone or to any other more commonly assigned causes but rather to the effect of an unrecognized toxin on capillary permeability. Wilder,[21] on the other hand, maintained that a hemorrhagic lesion of the retina associated with diabetes is an expression of a vascular disease unrelated etiologically to the metabolic disturbances of diabetes. Were it otherwise, a larger proportion of patients with uncomplicated diabetes should show this abnormality.

Bedell [22] expressed the opinion that probably all observers agree that with the exception of the peculiar condition called lipaemia retinalis lesions of the eyegrounds do not develop in children even though they succumb to diabetes. It seems clear, therefore, that the age of the patient, the duration of the disease and the severity of the pancreatic involvement with the resulting damage to the blood vessels are the essential factors in the production of the lesions in the fundus.

Gray [23] concluded that a characteristic form of retinitis frequently exists in cases of diabetes and begins in the central part of the retina as whitish yellow spots. He expressed the belief that the small amount of sclerosis of the retinal vessels is an important point of differentiation from retinitis of other origin. Hemorrhages may be due to the effect of a toxin causing secondary changes in the vessels or to hypertension (the latter being probably a secondary mechanical factor).

Šafář [24] discussed the various disturbances and changes that take place in the eye in cases of diabetes and stated that symptoms are due only partially to disturbance in metabolism, changes in the blood vessels also playing a part.

Vom Hofe [25] found an increase of blood pressure in the majority of patients with diabetic retinal changes. He observed that in most cases the patients are not young and the diabetes has been present more than five years. From the metabolic disturbances in diabetes there occur injuries to the vessels leading to nutritional disturbances of the retinal tissue.

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20. Waite, J. H.: Ocular Complications Found in the Study of Two Thousand Diabetic Patients, Arch. Ophth. **12**:143 (July) 1934.

21. Wilder, R. M., in Symposium on Ocular Complications of Diabetes, Arch. Ophth. **12**:144-146 (July) 1934.

22. Bedell, A. J., in discussion on Wilder.[21]

23. Gray, W. A.: The Ocular Conditions in Diabetic Mellitus, Brit. J. Ophth. **17**:577-620 (Oct.) 1933; abstracted, Arch. Ophth. **12**:431 (Sept.) 1934.

24. Šafář, K.: Diabetes and the Eye, Wien. med. Wchnschr. **88**:685-687 (June 18) 1938; abstracted, Am. J. Ophth. **22**:113 (Jan.) 1939.

25. vom Hofe, K.: Changes in the Fundus from Diabetes, Arch. f. Ophth. **139**:801-810, 1938; abstracted, Am. J. Ophth. **22**:466 (April) 1939.

Cohen [26] in his latest paper maintained his opinion expressed eight years previously [11] that diabetes occurs at a time when arteriosclerosis is likely to be present and that the bilateral changes in the fundus are so well known that they require no comment except that the retinal vessels show definite evidence of varying degrees of arteriosclerosis. Hypertension, if present secondarily, is likely to aggravate the lesion of the fundus. Agreeing with others who have studied so-called diabetic retinitis, he stated that this lesion is due mainly to sclerosis of the retinal and choroidal blood vessels and that the disturbance of the sugar metabolism, as he has previously reported, is contributory only under certain conditions. Cohen definitely concluded that hypertension and arteriosclerosis are frequently associated with diabetes and that the retinal arteriosclerosis is part of the general arteriosclerosis. These findings led Cohen to believe that so-called diabetic retinitis is due mainly to arteriosclerosis of the retinal and choroidal blood vessels and that in some instances diabetes may influence the picture, particularly in the cases in which the disease is protracted. Diabetic retinitis should therefore be called retinal arteriosclerosis (moderate or severe) associated with diabetes rather than diabetic retinitis. There are a few authors who believe that diabetic retinitis exists as an entity and is not dependent on vascular changes. Gradle [9] stated: "Foster Moore was practically the only authority today who maintained that there was such an entity as diabetic retinitis."

An interesting case report was that by Adams.[27] The patient, who was diabetic, was 22 years old. The right eye had yellowish areas of retinitis at the macula and one mossy retinal hemorrhage. In the left eye there were no obvious signs of the disease in the retinal blood vessels, though there were mossy and punctate hemorrhages. The systolic blood pressure was 100 and the diastolic 75. Koyanagi [28] in his series of 15 cases of diabetic retinitis reported that in more than half of them the maximal systolic blood pressure did not exceed 150 mm. of mercury. This fact and the spontaneous subsidence of the retinal changes in 2 cases argued against the angiospastic theory.

Mukerjee,[29] after the usual discussion of ocular complications of diabetes, questioned the statement that retinal diabetic changes are due

26. Cohen, M.: Lesions of the Fundus in Essential Hypertension and in Arterial and Renal Diseases, Arch. Ophth. **17**:994-1007 (June) 1937.

27. Adams, P. H.: Diabetic Retinitis in a Patient Aged Twenty-Two, Brit. J. Ophth. **16**:38-39 (Jan.) 1932; abstracted, Arch. Ophth. **7**:638 (April) 1932.

28. Koyanagi, Y.: Does Hypertony Play an Essential Part in Diabetic Retinitis? Klin. Monatsbl. f. Augenh. **94**:355-366 (March) 1935; abstracted, Am. J. Ophth. **18**:679 (July) 1935.

29. Mukerjee, S. K.: Ocular Affections in Diabetes, Proc. All-India Ophth. Soc. **4**:86-94, 1935; abstracted, Am. J. Ophth. **19**:1143 (Dec.) 1936.

to concomitant renal defects. Hanum's [30] careful studies fail to show that diabetic retinitis is dependent on renal changes, hypertension or disturbances in blood chemistry.

Gasteiger [31] in his discussion of the paper by Braun [32] maintained that one must agree with Mylius that increased blood pressure is not to be considered the decisive etiologic factor in diabetic retinitis.

Braun [33] stated that the retinitis is caused by the diabetic alterations of tissue metabolism, i. e., chiefly by the acidosis and ketonemia, and that the vascular changes and hypertension are, contrary to the common belief, not primary. In some of his cases the retinitis seemed to be related to renal insufficiency.

The series of patients reported on in this study were all personally observed in the metabolic department of the Philadelphia General Hospital during my service as resident ophthalmologist. The patients were all under the care of Drs. E. S. Dillon and A. Sindoni Jr., of the metabolic division, and were seen in routine examination. One hundred patients were studied, 95 of whom were resident patients, the remaining 5 at the time of examination being outpatients, having been resident patients of the metabolic division at an earlier date. For the metabolic data we are indebted to the department of metabolism.

For the purpose of brevity the pertinent data (according to age groups) have been assembled in the tables.

SUMMARY OF DATA IN TABLE 1

The youngest patient in this group was 1 year of age, and the oldest was 39.

The shortest known duration of the disease was two weeks (in the youngest patient of the group), and the longest known duration was fifteen years (in a patient aged 17).

As has been indicated, for 13 of the 29 patients the urine contained albumin (from a trace to 3 plus). In none of these was there any change in the fundus.

Six of the patients (cases 18, 19, 21, 22, 24 and 28), as is indicated in the table, had a systolic pressure of 140 mm. of mercury or greater; none was found to have any retinal changes.

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30. Hanum, S.: Diabetic Retinitis, Acta ophth., 1939, supp. 16, pp. 3-174; abstracted, Am. J. Ophth. **22**:804 (July) 1939.

31. Gasteiger, H., in discussion on Braun.[32]

32. Braun, R.: Insulin and the Eye, Arch. Ophth. **18**:860 (Nov.) 1937.

33. Braun, R.: Diabetic Retinitis: A Study of One Hundred and Fifteen Cases, Arch. f. Ophth. **136**:256-302, 1936; abstracted, Arch. Ophth. **18**:167 (July) 1937.

TABLE 1.—*Data on Group Aged 1 to 39, Inclusive (Total, 29 Patients)*

A. 13 cases. No albumin and no changes in fundus
B. 13 cases. Trace of albumin to 3 plus; no changes in fundus
C. 3 cases. No urinalysis and no changes in fundus

According to age: Lowest, 3½ years (blood pressure, 52/26)*
Highest, 30 years (blood pressure, 158/98)

According to blood pressure: Lowest, 52/26 (patient's age 3½ years)
Highest, 178/80 (patient's age 30 years)

Case	Age, Years	Duration	Blood Pressure	Vessels	Fundus	Electrocardiogram	Diagnosis
A.							
1	1	2 wk.	Not taken	Normal	No lesions	None	Diabetes
2	3½	2 yr.	52/26	Normal	No lesions	None	Diabetes; acidosis
10	17	4 yr.	108/60	Normal	No lesions	Nothing abnormal	For standardization
11	17	3 yr.	108/70	Normal	No lesions	None	Diabetes with mild acidosis
13	18	10 yr.	110/78	Normal	No lesions	None	For standardization
14	20	3 yr.	120/75	Normal	No lesions	None	For standardization
15	22	6 mo.	122/70	Normal	No lesions	None	Diabetes
16	23	12 yr.	122/80	Normal	No lesions	None	Diabetes; pregnancy
17	24	5 yr.	128/78	Tortuous	No lesions	None	Diabetes; left lobar pneumonia
19	29	8 yr.	166/96 to 122/70	Normal	No lesions	Normal except for tachycardia	Diabetes; gangrenous appendix
25	34	3 yr.	112/80	Arteries slightly sclerotic and slightly compressed	No lesions	None	Diabetes
27	39	12 yr.	130/70	Arteries slightly sclerosed; no compression	No lesions	None	Diabetes; acute respiratory infection
28	39	5 yr.	152/98	No sclerosis	No lesions	No significance	Diabetes; standardization
B.							
4	14	4 yr.	108/78	Normal	No lesions	None	Diabetes; acidosis
5	14	4 yr.	100/60	Normal	No lesions	None	Diabetes; acidosis
6	16	5 yr.	138/70	Normal	No lesions	None	Diabetes; acidosis
7	16	10½ yr.	98/74	Normal	No lesions	None	Diabetes; acidosis
8	17	9 yr.	94/70	Normal	No lesions	None	Diabetes; acidosis
9	17	15 yr.	134/84	Normal	No lesions	None	Diabetes; acidosis
12	17	7 yr.	110/70	Normal	No lesions	None	Diabetes; tuberculosis
18	26	7 yr.	140/80	Normal	No lesions	None	Diabetes; mild acidosis
20	29	5 yr.	106/60	Normal	No lesions	None	Diabetes; diarrhea unknown cause
21	30	2 yr.	150/50 to 110/68	Normal	No lesions	None	Diabetes; coma
22	30	2 yr.	178/80	Arteries reduced in caliber and with marked compression	No lesions	None	Diabetes; hypertension
23	31	2 mo.	110/66	Normal	No lesions	None	Diabetes with acidosis
26	36	12 yr.	108/70	Arteries slightly sclerotic and tortuous; no compression	No lesions	None	Diabetes; pregnancy
C.							
3	8	8 mo.	Not taken	Normal	No lesions except periphery shows fine powdery pigment-like deposits in O^2	None; Wassermann negative	Standardization
24	32	3 yr.	160/104 to 140/80	Arteries appear sclerotic; no compression	No lesions	None	Diabetes; acute respiratory infection
29	39	1 yr.	128/80	Arteries tortuous, sclerotic and with slight compression	No lesions	None	Diabetes; acute nasopharyngitis

* The blood pressure of the youngest patient, aged 1 year, was not determined.

TABLE 2.—*Data on Group Aged 40 to 49, Inclusive (Total, 18 Patients)*

A. 4 cases. No albumin; no changes in fundus
B. 7 cases. Albumin; no changes in fundus
C. 7 cases. Albumin; changes in fundus

According to age: Lowest, 40 years (blood pressure, 120/60)
Highest, 49 years (blood pressure, 126/82)

According to blood pressure: Lowest, 112/74 (patient's age, 47)
Highest, 238/124 (patient's age, 47)

Case	Age	Duration	Blood Pressure	Vessels	Fundus	Electrocardiogram	Diagnosis
A.							
33	40	1½ yr.	120/80	Arteries slightly sclerosed, with slight compression	No lesions	None	Diabetes; diabetic emaciation
37	44	5 yr.	128/80	Arteries slightly sclerosed, with slight compression	No lesions	None	Diabetes; chronic prostatitis
40	45	No history	114/62	Arteries reduced in caliber, tortuous, with slight compression	No lesions	None	Diabetes; hemorrhoids
45	48	11 yr.	120/60	Arteries slightly sclerosed with slight compression	No lesions	None	Diabetes; grip
B.							
30	40	10 yr.	196/130	Arteries suggest sclerosis; no compression	No lesions	None	Diabetes
31	40	3 yr.	120/60	Normal	No lesions	No significance	Diabetes; acidosis
36	43	9 yr.	118/78	Arteries slightly sclerotic, but no compression	No lesions	None	Diabetes; acidosis
38	45	12 yr.	110/50	Arteries somewhat sclerotic, but no compression	No lesions	Normal	Diabetes
39	45	7 yr.	120/70	Arteries sclerotic, with slight compression	No lesions	None	Diabetes; cold
41	46	1 yr.	132/84	Arteries reduced in caliber, with sclerosis; slight compression	No lesions	Suggestive, but depends on other clinical picture	Diabetes; acidosis

	42	47	8 yr.	136/76	Arteries sclerotic; marked compression	No lesions	None	Diabetes; gangrene
C.	32	40	3 yr.	180/112 to 118/80	Sclerotic and constricted	White exudates scattered throughout; no change in macula	Myocardial derangement	Diabetes; hypertensive cardiovascular disease
	34	41	3 yr.	148/80 to 174/106	Advanced sclerosis	Recent and old massive moderate-sized superficial and deep hemorrhages scattered throughout fundus; large area of white exudate involving macula, more widespread in left eye	Nothing abnormal	Diabetes; arterial hypertension
	35	43	7 yr.	138/88	Sclerotic; no compression	Patch of exudate above disks O^2	Definite myocardial disease	Diabetes
	43	47	No history	238-124	Sclerotic with compression	Right eye: white exudates throughout fundus; macular area shows some deposits. Left eye exudates less	Marked myocardial degeneration	Diabetes; hypertensive cardiovascular disease
	44	47	8 yr.	112/74	Slight sclerosis; no compression	Right eye: pinpoint exudates above and below disk. Left eye: no lesions. Trauma to right eye 12 years ago	None	Diabetes; shock
	46	49	2½ yr.	180-100	Sclerotic with marked compression	Right eye: hard white exudates, irregular sizes scattered throughout fundus; no hemorrhages. Left eye: hemorrhages and exudates	Myocardial degeneration	Diabetes
	47	49	1 yr.	126/82	Sclerotic, with slight compression	Right eye: fine hemorrhages in fundus and macular area; few white exudates. Left eye: hemorrhages but no exudates	Not conclusive	Diabetes; otitis media

From the foregoing data on group 1 (29 cases) the following conclusions can be drawn:

1. There were no changes in the fundus in patients below 40 years of age.
2. There were no changes in the fundus in patients whose urine contained albumin from a trace to 3 plus.
3. There were no changes in the fundus related to the duration of the diabetes. (The shortest known duration was two weeks; the longest, fifteen years, and the average, five and one-third years.)
4. There were no changes in the fundus in patients whose systolic pressure was 150. The electrocardiogram in 2 cases did not show anything abnormal. In 1 case the systolic pressure was 178, with sclerosis of the vessels but no other lesions.
5. In 29 cases (100 per cent) no changes in the fundus were noted.

SUMMARY OF DATA IN TABLE 2

The youngest patient was 40 and the oldest was 49. The shortest known duration of the disease was one and one-half years. The longest known duration was twelve years (in a patient 45 years old). The average known duration in 16 cases was five and three-fourths years. Two patients had no knowledge of the presence of diabetes.

The following data were obtained:

1. Four patients without albuminuria definitely showed no changes in the fundus.
2. Seven patients with albuminuria definitely showed no changes in the fundus. In these the arteries were slightly sclerotic and compressed, except in 1 (case 42), whose arteries showed marked compression. Three of the 7 patients were studied by electrocardiogram, with negative results.
3. Seven patients with albuminuria all showed changes in the fundus. Four of the seven patients showed myocardial changes when examined electrocardiographically. The electrocardiogram of 1 patient showed nothing abnormal, and that of another, nothing conclusive. The remaining patient was not studied by this means. This patient had been struck in the right eye twelve years previously. Is this significant?

The following conclusions may be drawn:

1. The percentage without any changes in the fundus was 61.
2. The percentage with changes in the fundus was 39.
3. In a group of 7 patients with albuminuria and changes in the fundus there were 4 (57.2 per cent) in whose cases the changes were confirmed by electrocardiographic signs of derangement of

the vascular system; there were 2 (28.5 per cent) in whose cases the changes were not confirmed by electrocardiogram, and there was 1 (14.3 per cent) in whose case no electrocardiogram was taken.

SUMMARY OF DATA IN TABLE 3

The youngest patient in this group was 50 years of age, and the oldest was 59. The shortest known duration of the disease was 1 month (case 62). The longest known duration was 35 years (case 72). The average known duration in 21 of 25 cases was eight and two-tenths years.

In 2 cases the duration was unknown. In 1 case the disease had been known to be present for several months, and in 1 case, for years.

The following data were obtained:

1. The 6 patients without albuminuria definitely did not show any lesions of the fundus. Two of these 6 had marked compression. In the electrocardiogram case 54 did not confirm the presence of myocardial disease, on account of digitalis. In case 57 the electrocardiogram suggested myocardial derangement.
2. In 3 patients not studied by urinalysis there were no changes in the fundus. In case 69 the electrocardiogram confirmed the myocardial change (probably hyperarteriosclerosis).
3. Four patients had albuminuria and no changes in the fundus. In case 60 the electrocardiogram confirmed the presence of arteriosclerotic heart disease with hypertension.
4. Ten patients had albuminuria and changes in the fundus. In 5 cases the electrocardiogram showed confirmatory myocardial changes. In 4 it revealed no myocardial changes. In 1 an electrocardiogram was not taken.
5. One patient had no albuminuria but showed changes in the fundus. The electrocardiogram did not show disease (case 64).
6. One patient who was not studied by urinalysis had changes in the fundus. The electrocardiogram indicated myocardial disease (case 52).

The following conclusions may be drawn:

1. The percentage without any changes in the fundus was 52. The percentage with changes in the fundus was 48.
2. In a group of 13 patients without any changes in the fundus, 3 (23 per cent) showed myocardial involvement confirmed by electrocardiogram. Four (31 per cent) were studied electrocardiographically, without evidence of myocardial disease. Six (46 per cent) were not studied by this means.

TABLE 3.—*Data on Group Aged 50 to 59, Inclusive (Total, 25 Patients)*

A. 6 cases. No albumin and no changes in fundus
B. 3 cases. No urinalysis and no changes in fundus
C. 4 cases. Albumin and no changes in fundus
D. 10 cases. Albumin and changes in fundus
E. 1 case. No albumin but changes in fundus
F. 1 case. No urinalysis but changes in fundus

According to age: Lowest, 50 (blood pressure, 120/72)
Highest, 59 (blood pressure, 138/80)

According to blood pressure: Lowest, 108/56 (patient's age, 52)
Highest, 200/100 (patient's age, 58)

	Case	Age	Duration	Blood Pressure	Vessels	Fundus	Electrocardiogram	Diagnosis
A.	48	50	5 yr.	130/90	Sclerosed, with slight compression	No lesions	None	Diabetes; perirectal abscess
	50	50	11 yr.	120/72	Sclerosis but no compression	No lesions	Normal	Diabetes; osteomyelitis
	53	52	17 yr.	108/56	Sclerosis, with slight compression	No lesions	None	Diabetes; grip
	54	52	7 yr.	146/80	Sclerosis, with marked compression	No lesions	Does not confirm myocardial disease on account of digitalis	Diabetes; arteriosclerotic heart disease
	57	54	Unknown	176/90	Arteries threadlike, with marked compression	No lesions	Suggests myocardial derangement	Diabetes; hypertension
	63	56	4 mo.	100/72	Slight sclerosis, with slight compression	No lesions	Nothing abnormal	Diabetes; mild double hernia
B.	55	53	1½ yr.	180/100	Slight sclerosis; no compression	No lesions	None	Diabetes; cardiovascular disease
	58	54	Several months	108/70	Slight sclerosis; slight compression	No lesions	Nothing abnormal	Diabetes; appendical abscess
	69	58	2 mo.	200/100	Slight sclerosis; slight compression	Right eye: no hemorrhages, exudates or macular changes. Left eye: mature cataract; unable to see fundus	Myocardial change, probably hyperarteriosclerosis	Diabetes; hypertension; general arteriosclerosis
C.	49	49	14 yr.	170/100	Sclerotic and tortuous; slight compression	No lesions	None	Diabetes; hypertension; cellulitis
	51	50	For years	138/84 to 112/62	Sclerotic, with slight compression	No lesions	None	Diabetes with acidosis

	60	55	6 yr.	170/96	Sclerotic, with slight compression	No lesions	Arteriosclerotic, with hypertension	Diabetes
	66	57	7 yr.	172/94 to 140/90	Sclerotic; no compression	No lesions	None	Diabetes; hypertensive cardiovascular disease; infected foot
D.	56	53	13 yr.	116/86	Arteries reduced in caliber, sclerotic, some compression	Right eye: macular area shows beginning changes. Left eye: few pinhead hemorrhages; macular area has more changes	Arteriosclerosis	Diabetes; gangrene; general arteriosclerosis with arteriosclerotic heart disease
	59	55	10 yr.	140/68	Arteries sclerotic, with slight compression	Right eye: few hard, white exudates in macular region. Left eye: no changes	Permanent change in myocardium	Diabetes; hypertension; arteriosclerotic heart disease; infected foot
	61	55	6 mo.	168/80 to 158/100	Arteries sclerotic, with compression	Right eye: some pinpoint white exudates in fundus; no hemorrhages; macular area clear. Left eye: no lesions		
	62	55	1 mo.	160/80	Arteries sclerotic, with compression	Right eye: no exudates, no hemorrhages; macular area shows 3-4 pinhead exudates. Left eye: few pinhead hemorrhages, scattered; no exudates; macula clear	Nothing abnormal	Diabetes; hypertensive cardiovascular disease; infected right toe
	65	57	6 yr.	180/90	Arteries sclerotic, with compression	Right eye: numerous hard white exudates and hemorrhages scattered throughout; exudates about macular region also. Left eye: same	No conclusion	Diabetes; carcinoma of cervix
	67	57	8 yr.	134/80	Arteries sclerotic; marked compression	Right eye: numerous hard white exudates with old hemorrhages between; macula shows exudates. Left eye: exudates more extensive; no hemorrhages; macula shows changes	Myocardial degeneration	Diabetes; hemiplegia

TABLE 3.—*Data on Group Aged 50 to 59, Inclusive (Total, 25 Patients)—Continued*

	Case	Age	Duration	Blood Pressure	Vessels	Fundus	Electrocardiogram	Diagnosis
	68	58	3 yr.	156/96	Arteries sclerotic, with moderate compression	Right eye: ½ disk diameter nasal to disk, one hard exudate seen; no others present; no hemorrhages; macula clear. Left eye: no exudates	Normal	Diabetes; hypertrophy of prostate
	70	59	Unknown	138/80	Arteries sclerotic, with marked compression	Right eye: no exudates; irregular hemorrhages 1 disk diameter below disk; no changes in macula. Left eye: no lesions	Definite myocardial disease	Diabetes; hypertensive cardiovascular disease with decompensation
	71	59	6 yr.	166/72	Arteries sclerotic, with slight compression	Right eye: pinpoint hemorrhages and exudates scattered throughout; some in macular area. Left eye: more hemorrhages present; no exudates	Nothing abnormal	Diabetes; cholecystitis; chronic cholelithiasis
	72	59	35 yr.	156/94	Arteries sclerotic, with marked compression	Right eye: pinhead hemorrhages and yellow exudates scattered throughout fundus; hemorrhage at macular area. Left eye: hemorrhages and exudates less numerous	Myocardial derangement	Diabetes; hypertensive cardiovascular disease; infected callus
E.	64	57	10 yr.	116/66	Arteries sclerotic, with slight compression	Right eye: no lesions except a small patch of choroiditis 2 disk diameters nasal to disk. Left eye: no lesions and no choroiditis	Does not show disease	Diabetes; arteriosclerosis
F.	52	51	1 yr.	146/76	Arteries sclerotic, with slight compression	Right eye: few pinhead hemorrhages throughout; hard white exudates present; macula with hemorrhages. Left eye: no hemorrhages, but exudates scattered throughout; macula shows few exudates and hemorrhages	Damaged heart by coronary occlusion	Diabetes; controlled arteriosclerosis; infected foot; intermittent claudication

3. In a group of 12 patients with changes in the fundus, there were 6 (50 per cent) in whose cases the changes were confirmed by electrocardiographic evidence of myocardial disease; there were 5 (41 per cent) in whose cases the electrocardiogram yielded no confirmatory evidence, and there was 1 (9 per cent) in whose case no electrocardiogram was taken.

SUMMARY OF DATA IN TABLE 4

The youngest patient was 60 years of age, and the oldest was 69. The shortest known duration of the disease was represented by a case in which it was discovered at the time of examination. In 2 cases the duration was unknown.

The longest known duration was 27 years, in a patient aged 69. The average known duration (in 19 of the 22 cases) was six and nine-tenths years.

The following data were obtained:

1. Four patients without albuminuria definitely did not show any changes. The most remarkable patient was a woman (case 87) who had taken as much as 900 units of insulin and who was required to take 520 units to prevent acidosis.
2. In a group of 9 patients with albuminuria and no changes in the fundus there were 4 (44.4 per cent) in whose cases the electrocardiogram showed confirmatory myocardial changes; there were 3 (33.3 per cent) in whose cases no confirmatory evidence was revealed by electrocardiogram, and there were 2 (22.3 per cent) who were not studied electrocardiographically.
3. In a group of 7 patients with albuminuria and changes in the fundus there were 6 in whose cases the electrocardiogram confirmed the presence of myocardial changes and 1 who was not studied electrocardiographically.
4. Two patients in whom urinalysis was not done had changes in the fundus. In both instances the electrocardiogram confirmed the presence of myocardial disease.

The following conclusions may be drawn:

The percentage without any changes in the fundus was 59.

The percentage with changes in the fundus was 41.

In a group of 13 patients without changes in the fundus, 5 (38.5 per cent) were not studied electrocardiograpically; in the cases of 5 (38.5 per cent) confirmatory evidence was obtained by electrocardiogram, and in the cases of 3 (23 per cent) the electrocardiogram furnished no confirmation.

TABLE 4.—*Data on Group Aged 60 to 69, Inclusive (Total, 22 Patients)*

A. 4 cases. No albumin; no changes in fundus
B. 9 cases. Albumin; no changes in fundus
C. 7 cases. Albumin; changes in fundus
D. 2 cases. No urinalysis; changes in fundus

According to age: Lowest, 60 (blood pressure, 120/90)
Highest, 69 (blood pressure, 135/84)

According to blood pressure: Lowest, 118/78 (patient's age, 64)
Highest, 211/114 (patient's age, 62)

	Case	Age	Duration	Blood Pressure	Vessels	Fundus	Electrocardiogram	Diagnosis
A.	74	60	Discovered now	136/80	Arteries slightly sclerosed, with slight compression	No lesions	None	Diabetes; lobar pneumonia; toxic hepatitis
	81	64	8 mo.	136/70	Arteries slightly sclerosed, with slight compression	No lesions	None	Mild diabetes
	87	67	12 yr.	186/96 to 130/76	Arteries slightly reduced in caliber; slight compression	No lesions	None; takes 900 units of insulin; 520 units to prevent acidosis	Diabetes; hypertensive cardiovascular disease; arteriosclerosis
	92	69	4 mo.	176/76	Arteries slightly sclerotic, with some compression	No lesions	Marked arterio-sclerosis	Diabetes; hypertensive cardiovascular disease; gangrene
B.	75	61	Unknown	138/88 to 156/96	Arteries sclerotic with marked compression	No lesions	None	Diabetes; mild acidosis
	76	62	7 yr.	200/80	Arteries sclerotic, with some compression	No lesions	Hypertension and myocardial disease	Diabetes; arteriosclerotic heart disease
	79	63	1½ yr.	130/70	Arteries slightly sclerotic, with compression	No lesions	Shows auricular fibrillation	Diabetes; arteriosclerotic heart disease
	80	63	3 yr.	140/60	Arteries reduced in caliber and sclerotic, with slight compression	No lesions	Against cardiac origin	Diabetes; general arterio-sclerosis; arteriosclerotic heart disease; hypertension
	82	64	Unknown	118/.8	Arteries reduced in caliber; no compression	No lesions	Nothing abnormal	Diabetes; acute cholecystitis
	85	65	6 yr.	150/100	Arteries slightly sclerotic, with slight compression	No lesions	Definite myocardial change	Diabetes; hypertensive cardiovascular disease; mucous fistula (postoperative)
	89	68	2 yr.	170/80	Arteries markedly sclerotic, with marked compression	No lesions	For 5 years no change	Diabetes; hypertensive cardiovascular disease
	91	68	2 yr.	184/82	Arteries sclerotic, with no compression	No lesions	Some myocardial disease	Diabetes; hypertensive cardiovascular disease
	93	69	27 yr.	136/84	Arteries sclerotic, with marked compression	No lesions	None	Diabetes; cerebral vascular thrombosis; otitis media
C.	73	60	8 yr.	120/90 to 110/80	Arteries reduced in caliber, with marked compression	Right eye: yellowish white exudates scattered throughout; no hemorrhages seen; white hard exudates about macular area. Left eye: soft yellowish exudates scattered here and there; no hemorrhages; macular area shows beginning changes	Advanced myocardial disease	Diabetes; arteriosclerotic heart disease with failure

hemorrhages; macular area shows beginning changes

	77	62	7 yr.	216/114	Veins full; arteries reduced in caliber, with compression	Right eye: macular area shows exudates and some scattered throughout fundus; no hemorrhages. Left eye: same, with exudates scattered throughout	Myocardial derangement	Diabetes; hypertensive cardiovascular disease; general arteriosclerosis
	78	63	12 yr.	158/96	Veins full; arteries sclerosed, with some compression	Right eye: few small irregular hemorrhages scattered about; no exudates; no macular changes. Left eye: hemorrhages present; below macula are small yellowish exudates; nothing seen outside	Because of long-standing diabetes there is very likely some coronary arteriosclerosis	Diabetes; arteriosclerosis; gangrene
	83	65	3 yr.	150/80	Arteries reduced in caliber; markedly sclerotic, with slight compression	Right eye: small, hard, white exudates scattered throughout; macula shows some changes; no hemorrhages. Left eye: same, with small hemorrhages; macula with beginning exudates	Suggests branch block	Diabetes; arteriosclerotic heart disease; infected foot
	86	65	1 yr.	140/90	Veins full; arteries sclerotic, with marked compression	Right eye: soft, white exudates scattered throughout; hemorrhages; macula shows pinhead exudates and hemorrhages. Left eye: ocasional exudate; no hemorrhages; no changes in macula	Arteriosclerosis and hypertension	Diabetes; arteriosclerotic heart disease
	88	67	3 yr.	138/68 to 160/70	Veins full; arteries reduced in caliber and sclerotic, with marked compression	Right eye: pinhead hemorrhages; no exudates; macula shows white deposits. Left eye: same	None	Diabetes; bronchopneumonia, malnutrition
	94	69	15 yr.	178/72	Arteries sclerotic, with slight compression	Right eye: soft exudates throughout fundus; macula shows changes. Left eye: same	Arteriosclerotic heart disease	Diabetes; general arteriosclerosis; hypertensive cardiovascular disease
D.	84	65	3 yr.	190/110	Arteries sclerotic, with marked compression	Right eye: hemorrhages scattered throughout fundus; no exudates; no macular changes. Left eye: more hemorrhages	Advanced myocardial disease; acute occlusion	Diabetes; peripheral vascular disease; general arteriosclerotic heart disease; acute coronary occlusion; cardiac dilatation
	90	68	9 yr.	190/100	Arteries sclerotic, with marked compression	Right eye: deep and superficial hemorrhages throughout; no exudates; no macular changes. Left eye: hemorrhages (less extensive)	Confirms hypertension	Diabetes; primary pernicious anemia

TABLE 5.—*Data on Group Aged 70 to 77, Inclusive (Total, 6 Patients)*

A. 1 case. No albumin; no changes in fundus
B. 2 cases. Albumin; no changes in fundus
C. 3 cases. Albumin; changes in fundus

According to age: Lowest, 70 (blood pressure, 142/90)
Highest, 77 (blood pressure, 160/80)

According to blood pressure: Lowest, 120/70 (patient's age, 71)
Highest, 170/100 (patient's age, 70)

	Case	Age	Duration	Blood Pressure	Vessels	Fundus	Electrocardiogram	Diagnosis
A.	97	71	Not known	120/70	Arteries markedly sclerosed, with marked compression	No lesions	Auricular and ventricular extrasystoles	Diabetes; general arteriosclerosis; arteriosclerotic heart disease
B.	98	72	30 yr.	160/70	Arteries reduced in caliber, with slight compression	No lesions	Myocardial disease	Diabetes; general arteriosclerosis
	99	73	6 mo.	150/80	Arteries slightly sclerosed, with slight compression	No lesions	Advanced myocardial disease	Diabetes; gangrene
C.	95	70	6 yr.	170/100	Arteries sclerosed, with slight compression	Right eye: superficial and deep hemorrhages; hard, white exudates; no macular changes. Left eye: no hemorrhages, but a similar picture	Decompensation	Diabetes; hypertensive cardiovascular disease
	96	70	20 yr.	142/90	Arteries sclerosed, with slight compression	Right eye: numerous hard, white exudates; no hemorrhages; macula clear. Left eye: hard exudates and spokelike exudates in macular area	Myocardial degeneration clouded by digitalis	Diabetes; hypertensive cardiovascular disease; arteriosclerotic heart disease
	100	77	4 yr.	160/80	Veins reduced in caliber; arteries more so; arteries markedly sclerotic	Right eye: retinal thinning showing choroidal circulation; pigment present, with hard deposits scattered throughout; macula shows changes. Left eye: not seen; cataractous	No clinical conclusion	Diabetes; general arteriosclerotic heart disease

In a group of 9 patients with changes in the fundus, there were 8 (89 per cent) in whose cases the electrocardiogram confirmed the presence of myocardial disease and 1 (11 per cent) in whose case no electrocardiogram was taken.

In the total group of 22 cases there were 6 (27.2 per cent) in which no electrocardiogram was taken; 3 (13.8 per cent) in which the electrocardiogram yielded no confirmation, and 13 (59 per cent) in which confirmatory evidence was obtained by electrocardiogram.

SUMMARY OF DATA IN TABLE 5

The youngest patient in this group was 70 years of age, and the oldest was 77.

In 1 case the patient did not know that he had diabetes.

The longest known duration was thirty years. The average known duration was twelve and one-tenth years in 5 of the 6 cases.

The following data were obtained:

1. The 1 patient without albuminuria definitely showed no lesions in the fundus.
2. There were 2 patients with albuminuria and no changes in the fundus.
3. There were 3 patients with both albuminuria and changes in the fundus.

Therefore, the percentage without any changes in the fundus was 50. The percentage with changes in the fundus was 50.

In 5 cases (83.3 per cent) the electrocardiogram showed myocardial disease. In 1 case (16.7 per cent) the electrocardiogram failed to reveal myocardial disease.

GENERAL SUMMARY

There were no changes in the fundus in patients below the age of 40 years (table 1).

In the group listed in table 2 it is interesting to note that every patient with marked retinal disturbance had, in addition to different degrees of sclerosis, some abnormalities of blood pressure, but what is even more significant is that in every case except 2 the electrocardiogram showed myocardial degeneration.

In patients beyond the age of 50 (table 3) it is rare not to find retinal lesions of diabetes. In 6 cases there were typical retinal lesions of diabetes. In the majority of these the electrocardiogram revealed pathologic change.

In the group listed in table 4 the electrocardiograms revealed that in almost every case there was pathologic change in the heart and in the

vascular system. However, the cases were evenly divided as to the presence or absence of retinal changes. Sclerosis and hypertension were evident in every case. In 5 cases there were typical retinal lesions of diabetes.

The data in table 5 practically confirm those in table 4.

There were definitely no changes in the fundus in 69 per cent of the cases. Changes in the fundus were observed in 31 per cent.

Metabolic disturbance alone does not seem responsible for the retinal changes.

In the majority of cases of diabetic retinitis there was associated arteriosclerosis, hypertension, nephritis or a combination of these factors, frequently combined with myocardial degeneration.

DARK ADAPTATION

SOME PHYSIOLOGIC AND CLINICAL CONSIDERATIONS

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Measurements of dark adaptation have been done by innumerable investigators using many different technics ever since the classic description of the phenomenon was made in 1865 by Aubert.[1] It has been only within recent years, however, that any progress has been made toward understanding the process. The intricate nature of the photoreceptor mechanism and the complexity of the retinal mosaic, where sensitivity to light varies throughout the structure, have provided pitfalls which were completely ignored by the early workers, with a resulting obscuration of the process of adaptation. Today, with the proper apparatus, measurement of dark adaptation is a simple procedure which is assuming greater importance in both research and clinical work. The theoretic development of dark adaptation and the working out of a practical technic have been reported in the physiologic rather than the ophthalmologic literature, with the result that the clinical application of the modern technic is lagging behind.

It is the purpose of this paper to discuss briefly the physiologic requirements for the proper measurement of dark adaptation, to present some new data relevant to the fundamental physiology of dark adaptation and, finally, to present clinical data. Threshold measurements for light perception as well as the actual course of dark adaptation will be presented. These have been referred to heretofore as measurements of the "light sense." I prefer not to use this term. The perception of light is the fundamental retinal function; it is the capacity of the retina to refine and differentiate this fundamental sensation which makes possible visual acuity, discrimination of intensity and the other retinal capacities; hence, there is no "light sense" distinguishable as such.

MEASUREMENT OF DARK ADAPTATION

Dark adaptation tests are performed by measuring frequently the threshold for light perception after the exposure of the eye to a bright

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1. Aubert, H.: Physiologie der Netzhaut, Breslau, E. Morgenstern, 1865.

light. Early workers failed to control their measurements accurately, with the result that mistaken ideas became prevalent. It was recognized that the peripheral portion of the retina seemed to show a large range of adaptation which could not be demonstrated in the fovea; therefore, it was concluded that dark adaptation was a process of the peripheral rods of the eye and that the fovea could not dark adapt (this notion is still to be found in some textbooks). An oversimplified mechanistic picture was drawn, to the effect that the cones functioned in the light-adapted eye (photopic vision) and the rods in the dark-adapted eye (scotopic vision).

That cones as well as rods show dark adaptation was unmistakably demonstrated by Hecht in 1921.[2] He used a small test field which limited observations to the rod-free fovea. Dark adaptation of the cones proved to be a rapid process, taking place in a few minutes, as contrasted to the thirty minutes or so that the rod curve requires to level out. Kohlrausch[3] (1922) confirmed Hecht's measurements and demonstrated that in the peripheral portion of the retina, where both cones and rods are present, the dark adaptation curve showed two stages of adaptation: the first corresponded to the cone curve as demonstrated in the fovea, and the second and slower stage was the familiar drawn-out adaptation curve attributed to the rods.

With the proper technic both cone and rod adaptation may easily be demonstrated. The rather formidable array of requirements which must be met before dark adaptation can be properly measured may be thought by some to complicate the procedure unnecessarily. Actually they serve not to complicate dark adaptation but to simplify it. One of the first principles in investigation is to isolate carefully the phenomenon being studied in order to remove as many extraneous influences as possible. If this procedure can be followed the results obtained are physiologically simple, for they describe the isolated phenomenon and are most readily capable of simple physiologic interpretation. However, simplicity in procedure—in this case inadequacy in the apparatus used and failure to meet the specifications to be outlined—can produce only the opposite effect. The no longer relatively isolated phenomenon of dark adaptation is obscured in a maze of complexities brought on by inadequate retinal fixation, altering color temperatures of the test light and many other uncontrolled factors. It is for this reason that most of the data published on dark adaptation in clinical ophthalmology have failed to show duplicity of function and can no longer be considered reliable

2. Hecht, S.: The Nature of Foveal Dark Adaptation, J. Gen. Physiol. **4**: 113, 1921.

3. Kohlrausch, A.: Untersuchungen mit farbigen Schwellenprüfslichtern über den Dunkeladaptationsverlauf des normalen Auges, Arch. f. d. ges. Physiol. **196**: 113, 1922.

measurements. New "simple" technics and apparatus for dark adaptation are constantly being introduced. In the light of modern knowledge, these are usually grossly inadequate and at best are capable of providing merely a rough qualitative approximation. Only an apparatus that is quantitatively reliable and can clearly show the course of both cone and rod adaptation has a place in clinical ophthalmology today.

A. *Physiologic Requirements for Proper Measurement of Dark Adaptation.*—Hecht and Shlaer [4] have described the precautions which must be taken in order that accurate measurements be obtained. These will be discussed only briefly here, for they have been summarized in the ophthalmologic literature by McDonald.[5] Only when these requirements are met can a complete and valid picture of dark adaptation be achieved.

1. Adapting Light: The preliminary period during which the eye is exposed to the bright light is the period of light adaptation. The brightness and duration of the adapting light are important in determining the subsequent course of dark adaptation. The higher the intensity of the adapting light and the longer its duration (up to a certain point, when an equilibrium, or "stationary state," is reached), the more complete will be the bleaching of the photosensitive retinal pigment. Their regeneration too will be slower. The subsequent adaptation (which is taken to be the measurable aspect of this regeneration) will also be slower.[6] When the adapting intensity is too weak, the cone adaptation curve becomes less prominent; finally, with still weaker adapting intensities the cone curve disappears, adaptation commencing within the rod range and leveling off fairly rapidly at the rod threshold.

2. Test Light: The other factors which must be controlled during the measurement of dark adaptation concern the test light with which the retinal sensitivity is measured. The most important requirement is to fix the retinal location studied, for sensitivity varies greatly over the retina and different threshold readings will be given at random if accurate fixation is not provided. The retina is most sensitive about 20 degrees peripherally; this corresponds to the retinal area where the population of rods is greatest. If an area close to the fovea is examined, the threshold will be much higher.

The area of illumination to which the retina is exposed is another factor to be controlled. The larger the test area, the lower is the

4. Hecht, S., and Shlaer, S.: An Adaptometer for Measuring Human Dark Adaptation, J. Optic Soc. America **28**:269, 1938.

5. McDonald, R.: Some Basic Principles of Dark Adaptation, Arch. Ophth. **23**:841 (April) 1940.

6. (*a*) Winsor, C. P., and Clark, A. B.: Dark Adaptation After Varying Degrees of Light Adaptation, Proc. Nat. Acad. Sc. **22**:400, 1936. (*b*) Hecht, S.; Haig, C., and Chase, A. M.: The Influence of Light Adaptation on Subsequent Dark Adaptation of the Eye, J. Gen. Physiol. **20**:831, 1939.

threshold. This factor is not as important as the retinal location of the test area; it has been shown that the greater part of the difference in threshold demonstrable for a 20 degree field and for a 3 degree field (centrally fixated) lies in the fact that the 20 degree field embraces more peripheral retinal areas, which are more sensitive. A 3 degree field peripherally fixated can give just as low a threshold.[7]

The time of exposure to the test light must be considered. The Bunson-Roscoe law governs the reciprocal relations between the intensity of illumination and the time of exposure of a flash of light: for a given brightness sensation the intensity times the exposure time is constant for exposure times up to about 0.2 second. For longer exposures than this the addition of more time is not effective in increasing the brightness of the flash.

Finally the color of the test light is important. For cone vision maximum visibility is at about 555 millimicrons in the yellow-green.[8] In achromatic rod vision the brightest spectral region is at about 510 millimicrons, which is in the green part of the spectrum. The difference between the cone and the rod visibility curve accounts for the familiar Purkinje phenomenon, the shift of visibility toward the blue end of the spectrum when brightness is diminished. The difference between the maxima of the two curves (which are reproduced in the article by McDonald [5]) causes a disparate relation between the two throughout the spectrum: At the violet end of the spectrum the separation is greatest; at the red end of the spectrum, on the other hand, the curves practically run together. In any spectral region the difference between the two curves indicates the photochromatic interval, when the light seen is colorless—the interval of intensity between the point where light is first perceived and the point where its color can be distinguished. This photochromatic interval indicates the range of intensity in which rod function can be measured independently of cone function. It is apparent that with the use of a violet test light the greatest range of rod function will be demonstrated; with a red test light only a very small rod range is possible. As a matter of fact, if the red light is limited to the extreme red end of the visible spectrum, no rod curve at all will appear. In dark adaptation measurements one is interested in demonstrating as well as it is possible both rod and cone function. Since the cone curve will not be affected by the color of the test light (unpublished data) and the rod curve will be maximum for violet, a violet test light is desirable. The violet test light will appear as violet during the first part of the adaptation period; below the cone threshold, however, when only rods

7. Hecht, S.; Haig, C., and Wald, G.: The Dark Adaptation of Retinal Fields of Different Size and Location, J. Gen. Physiol. **19**:321, 1935.

8. Hecht, S.: Rods, Cones and the Chemical Basis of Vision, Physiol. Rev. **17**:239, 1937.

are functioning, no color will be perceptible. With the red test light it is not possible under ordinary conditions to descend to an achromatic level. When it is desired to study only cone adaptation or to determine the cone threshold, a red filter may be used. This, for all practical purposes, will show only cone function.

Because of the relative changes between cone and rod sensitivity throughout the spectrum, it is of great importance that the spectral composition of the test light be held constant throughout the dark adaptation test. This is readily accomplished if the intensity of the test light is controlled by optical devices, as by the interposition of neutral filters and a photometric wedge. In some adaptometers, however, the brightness of the test light is cut down by means of rheostat. This results in a constantly changing color temperature of the test light. When the current is cut down, there is a definite shift toward the red end of the spectrum, particularly at the low illuminations with which it is necessary to work. An error is introduced into the dark adaptation data by this method.

3. Plotting Dark Adaptation Data: The manner of plotting the data obtained is very important. Early workers gave a value of unity to the original threshold measured immediately after the period of light adaptation; the reciprocals of subsequent thresholds were taken to indicate the increase in retinal sensitivity during dark adaptation. The fact that adaptation was proceeding most rapidly during the first moments in the dark and that therefore the first reading was particularly unreliable was ignored. With this method of plotting a small error in the first reading would throw the whole curve off.

Hecht [9] has pointed out the necessity of designating logarithmically the threshold illuminations perceived during dark adaptation. Threshold intensity may change over a range of 1 to 100,000 during dark adaptation. A tremendous ordinate scale would be required if the later and slower stages of adaptation, as measured by single units instead of tens of thousands of units, are to be measurable on the graph. This is rendered impractical by the size of paper required. If one were to contract the ordinate scale, adaptation would appear soon to be over, for a change in intensity from 100 to 1 would not be apparent in the figure. In a logarithmic plot, on the other hand, each unit signifies a tenfold change in intensity, whether this change is from 100,000 units to 10,000 or from 10 units to 1. This method is more correct physiologically. A change of 1 log unit in indicating a constant percentage change in the retinal sensitivity is directly applicable in a physiologic sense as indicating the regeneration of a definite percentage of visual purple. Therefore a logarithmic plot more closely reflects the

9. Hecht, S., and Mandelbaum, J.: The Relation Between Vitamin A and Dark Adaptation, J. A. M. A. **112**:1910 (May 13) 1939.

true picture of dark adaptation as it occurs in the eye. Hecht [8] replotted logarithmically the dark adaptation data obtained by Piper [10] in 1903. The data show clearly the division into a rapid (cone) and a slow (rod) component; this fact had been completely masked by the manner of plotting employed by Piper.

B. Apparatus and Method.—All these factors are controlled in the Hecht-Shlaer apparatus.[4] An adapting brightness of 1,500 millilamberts exposed to the eye for three minutes has been found to be most satisfactory when the natural pupil is used. Under these preadapting conditions a cone curve and a rod curve are clearly demonstrable. The rod curve levels off and adaptation is practically over by the end of thirty minutes (actually, adaptation may continue slowly for many hours at an extremely slow rate, but this is unimportant for clinical purposes).

A violet test light is used (Corning no. 511 violet filter) exposed in a 3 degree field for two-tenths second flashes. When only cone threshold readings are to be made, a red filter (Wratten no. 88) is used. For routine dark adaptation, the test light is exposed 7 degrees temporally to the fixation point, stimulating a retinal area where both cone and rod function are easily demonstrated. In earlier papers [11] describing these conditions the retinal area studied was described as 7 degrees nasal. In this paper the usual ophthalmologic terminology will be employed, nasal or temporal designating directions in the projected field, not on the retina.

Fixation is accomplished in the Hecht-Shlaer adaptometer by means of a small point of light. The brightness of the fixation light is kept at a minimum by means of a rheostat. This small light has no measurable effect on the dark adaptation of the peripheral retina. When its brightness is carefully maintained at a minimum, it does not even affect appreciably the threshold of central retinal areas.

A camera shutter adjusted for a fixed brief time exposes the test light to the eye when a reading is being made. Apart from the theoretic advantage of using a fixed time of exposure, another more practical and probably more important advantage is gained from the use of a camera shutter. Fixation is made much easier when the test light is exposed only for a brief flash; there are no peripheral distractions, and nothing is visible but the fixation point. The brief exposure period is over so rapidly that the fixation of the eye cannot be changed until it is over. Fixation is much more easily maintained by this method than with the customary perimetry technics.

Threshold readings are recorded logarithmically. In order to avoid negative logarithmic designations, a very small unit of brightness has been employed: the micromicrolambert (1 micromicrolambert is equal

10. Piper, H.: Ueber Dunkeladaptation, Ztschr. f. Sinnesphysiol. **31**:161, 1903.
11. Hecht and Shlaer.[4] Hecht and Mandelbaum.[9]

to 1 millilambert times 10^{-9}). Therefore, the data can be read off in terms of log millilamberts by subtracting 9 from the logarithmic ordinates or in micromillilamberts by subtracting 3.

C. Pupil Control.—The size of the pupil is an important factor in opthalmologic work in which pathologic or therapeutic conditions have altered the normal pupillary response. In subjects with normal pupillary reflexes this factor is not important; however, when one is dealing with a miotic pupil, the difference in threshold from that given by a normal pupil may exceed 1 log unit, a significant quantity.

Apart from influencing the level of the cone and rod thresholds, the presence or absence of an active pupil may alter the shape of the dark adaptation curve. During the first minutes of dark adaptation the pupil slowly relaxes, admitting more and more light through its aperture and thereby permitting progressively lower readings to be obtained apart from the state of adaptation of the retina. This effect occurs during the cone adaptation time; it is practically over by the time rod adaptation commences. The effect of the changing pupil on the shape of the cone curve is to prolong it slightly and to increase the speed of the first part of the curve; the total range of adaptation is increased by an amount corresponding to the extent of pupillary dilatation. The threshold level may appear to continue to decline slightly instead of actually leveling off after three or four minutes, as the pupil continues to dilate slightly.

The reactivity of the pupil is also of significance during the period of light adaptation, since the smaller the pupil, the less light is admitted to the retina and the lower the level of light adaptation achieved. During the three minutes of light adaptation a constant size of the pupil is not maintained, but a relaxation sets in after the original contraction. As Phillips [12] pointed out, the speed of dark adaptation is inversely proportional to the size of the pupil during light adaptation and directly proportional to the size of the pupil during dark adaptation. However, in normal persons differences produced by these effects are slight and not nearly sufficient to account for the range of variability in the shape of the curve or in the threshold level obtained. In ophthalmologic practice, on the other hand, when one is dealing with pupils that are fixed, as in miosis or mydriasis, either through a pathologic or a therapeutic process, it is necessary to correct data for pupil size. This factor has been recognized by most ophthalmologists who have worked with dark adaptation. Sloan [13] in her summary of the technics employed by various investigators listed the methods used.

12. Phillips, L. R.: Some Factors Producing Individual Differences in Dark Adaptation, Proc. Roy. Soc., London, s.B **127**:405, 1939.

13. Sloan, L. L.: Instruments and Technics for the Clinical Testing of the Light Sense: I. Review of the Recent Literature, Arch. Ophth. **21**:913 (June) 1939.

Since the pupil admits light in direct proportion to its area, correction factors which have been employed have been simply to reduce the area to a common denominator. However, Stiles and Crawford [14] have shown that the direct proportionality is invalid because light rays passing through the peripheral portions of the pupil are less efficient than rays passing through the center. This seemed to hold only for cone vision; for achromatic rod vision, as measured with violet light, the direct proportionality held. It was thought desirable to repeat this experiment with pupils of different diameters, instead of using the complex Maxwellian system these authors employed, in order to reproduce more closely the conditions that actually prevail during threshold measurements and in order to construct a chart that could readily be used in applying a correction factor to measurements of dark adaptation. These experiments were conducted with artificial pupils in the eyepiece of the apparatus, approximately 2 mm. in front of the cornea. Theoretically, this is different from a pupil of equal size in the pupillary plane of the eye. However, experiments made with carefully measured fixed pupils showed that this error was negligible and that the data obtained with artificial pupils could be used as applying to the natural pupillary plane.

Two trained observers [15] were used for this experiment. Their pupils were dilated with ophthalmic [15a] paredrine hydrobromide in order to accommodate easily the largest artificial pupil used. After twenty minutes of dark adaptation without any preceding light adaptation, threshold measurements were made first with a red test light and then with a violet test light. Six artificial pupils varying in diameter from 1 to 6.4 mm. were placed in the eyepiece of the apparatus; at least three measurements were made with each pupil. The test light was viewed centrally and 7 degrees temporally. The data obtained are reproduced in figure 1, in which the increment in ocular sensitivity obtained with the different pupils is plotted against the diameter of the pupils. The averages of the readings given by each observer for each artificial pupil are included within the shaded areas. The upper range includes the readings made with the violet test light; the lower range is for the red test light. The curve drawn through the data for the violet test light is the curve showing the relations between pupillary

14. Stiles, W. S., and Crawford, B. H.: The Luminous Efficiency of Rays Entering the Eye at Different Points, Proc. Roy. Soc., London, s.B **112**:428, 1933. Stiles, W. S.: The Luminous Efficiency of Monochromatic Rays Entering Eye Pupil at Different Points and New Colour Effect, ibid. **123**:90, 1937. Crawford, B. H.: Luminous Efficiency of Light Entering Eye Pupil at Different Points and Its Relation to Brightness Threshold Measurements, ibid. **124**:81, 1937.

15. Miss Harriet Sager assisted in all the experiments reported in the first two sections of this paper.

15a. Paredrine hydrobromide ophthalmic is a 1 per cent solution of *p*-hydroxy-α-methylphenethylamine hydrobromide in distilled water, made tear isotonic with 2 per cent boric acid and preserved with merthiolate, 1:50,000.

diameter and area; this curve fits my data well. For red light, on the other hand, the curve falls short of the direct relations. These results agree with the results of Stiles and Crawford. Sloan [16] failed to find any difference between the correction factor to be applied when red or violet light was used; in each case her correction factor agreed with the curve for pupillary area. However, the maximum difference between her correction factors and mine is only 0.2 log unit.

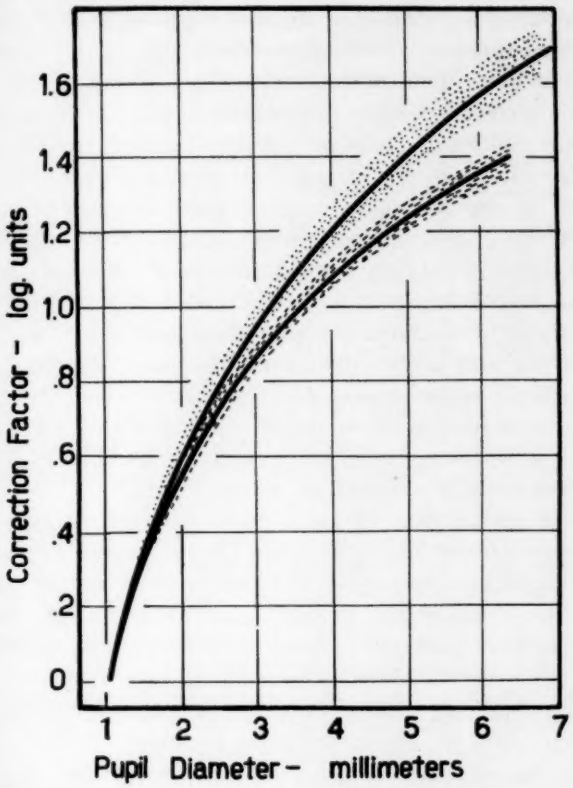


Chart 1.—Correction curves for size of pupil. The upper curve is for achromatic rod vision, measured with the violet test light, and the lower curve for chromatic cone vision, measured with the red test light.

The curves in chart 1 may be used for correcting the results obtained with any pupil from 1 to 6.4 mm. in diameter to a common level. *All the data to be presented in this paper are in terms of a 2 mm. pupil.* If

16. Sloan, L. L.: Instruments and Technics for the Clinical Testing of the Light Sense: IV. Size of Pupil as a Variable Factor in the Determination of the Light Minimum, Arch. Ophth. **24**:258 (Aug.) 1940.

it is desired to give the brightness in photons, the unit of retinal illumination, it is necessary only to subtract 8 from the logarithmic ordinates in micromicrolamberts, for with a 2 mm. pupil brightness in millilamberts times 10 equals brightness in photons.

The threshold values with the natural pupil and with a 2 mm. artificial pupil have been compared in 10 normal subjects. In no case did the difference vary by more than 0.1 log unit from 0.80 as the correction factor for cones and from 1.00 as the correction factor for rods. Therefore, in order to compare data obtained from subjects with normal pupillary reflexes with data obtained from subjects with fixed 2 mm. pupils or with data obtained when an artificial 2 mm. pupil is employed, it is necessary merely to add 0.80 to the cone threshold level and 1.00 to the rod level. It is permissible, then, to use the normally functioning natural pupil when miotics are contraindicated or when an artificial pupil is impractical, as long as these corrections are made.

As previously mentioned, the presence of an active pupil will affect somewhat the shape of the cone curve. In chart 2 curves are shown for the same subject with a normal (*A*) and with a 2 mm. artificial pupil (*B*). With the artificial pupil the cone threshold is 0.80 and the rod threshold 1.00 log unit higher than with the normal pupil. It can be seen that the change in the shape of the cone curve is only slight and not of importance in clinical measurements. The shape of the rod curve is not affected at all, because maximum pupillary dilatation has occurred by the time the rod curve commences.

The use of an artificial 2 mm. pupil inserted in the eyepiece of the apparatus proved impractical for clinical work because of the difficulty in exactly centering the eye. This method could be employed only with trained observers during experimental work and with unusually cooperative patients. Miosis obtained by the instillation of 2 drops of a 1 per cent solution of pilocarpine nitrate gave completely satisfactory results. This method fails to give absolutely uniform pupil sizes in different subjects; corrections must be made. Any pupillometer or device that will measure the pupil diameter to within 0.5 mm. will be sufficiently accurate. The error introduced by this approximation will be less than 0.2 log unit. In view of the wide normal threshold range and the great changes in sensitivity found in pathologic conditions and because of the inherent error in measurements of dark adaptation and the day to day variation of 0.3 log unit which was found to occur in normal persons, the error introduced by only approximate pupillometry is unimportant in clinical work. More accurate measurement of the pupillary aperture is not required.

Since with a miotic or fixed pupil secondary pupillary dilatation cannot occur during the period of light adaptation, less light reaches the retina and the level of light adaptation is lower. It is therefore necessary to use a brighter adapting light under these conditions in order to

produce the same level of adaptation. When a 2 mm. fixed or artificial pupil is used, an adapting intensity of 6,000 millilamberts is necessary in order to give dark adaptation curves similar in shape to the curves obtained with the natural pupil and a brightness of 1,500 millilamberts.

D. Normal Dark Adaptation.—When the necessary precautions are taken, dark adaptation data show a curve consisting of a rapid early portion attributed to cone adaptation and a slower secondary portion attributed to rod adaptation. Curve *B* in chart 2 is such a curve and was obtained from a normal subject with a 2 mm. artificial pupil. The shaded area in this figure shows the range of normal dark adaptation as given by 110 persons. These data as previously published (Hecht and Mandelbaum [9]) were for the normal pupil. Here they are corrected

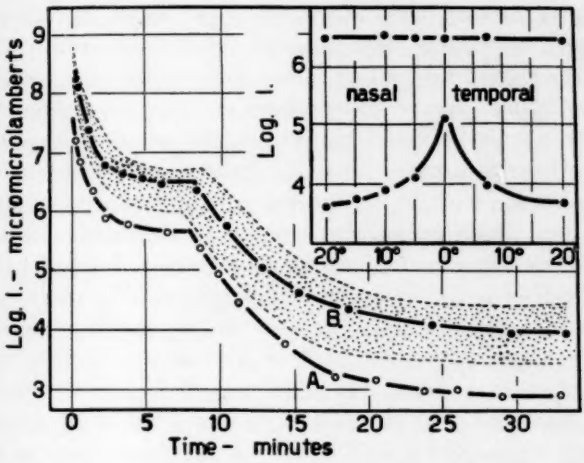


Chart 2.—Normal dark adaptation with a test light 3 degrees in diameter, violet and viewed 7 degrees temporally. Curve *A* is a normal dark adaptation curve not corrected for pupil size. Curve *B* was given immediately afterward by the same subject through a 2 mm. artificial pupil. The inset shows the contour of retinal sensitivity measured with a 3 degree test light along the horizontal meridian out to 20 degrees nasally and temporally. The upper curve shows the chromatic (cone) thresholds, measured with the red light, and the lower curve the achromatic (rod) thresholds, measured with violet light. This is the normal configuration and corresponds to curve *B*.

for pupil size and show the normal range when the pupil is 2 mm. in diameter. My clinical data can be compared directly with these normal figures. The normal distribution of rod thresholds extends over a range of 1 log unit; this is the same range of distribution that Ferree and Rand [17] found in 206 normal persons. We were able to find no correlation between the final rod threshold and the age of the subject, as has been

17. Ferree, C. E., and Rand, G.: Critical Values for the Light Minimum and for the Amount and Rapidity of Dark Adaptation, Brit. J. Ophth. **18**:673, 1934.

claimed by some observers. There was some tendency, however, for the level of the cone threshold to rise with age. It was found that normal persons showed a day to day variation which was as great as 0.3 log unit. This variation cannot be attributed to error in method, for if a dark adaptation test is repeated at the same time the curve will be found to agree closely with the original one. Also, it is not a matter of learning the technic, for similar variation is found whether the subject is a novice or an old hand at dark adaptation tests. The cause must be attributed to some variability in the receptivity of the nervous system or to instability of nutritional factors. When dark adaptation measurements are made on patients during clinical investigation it is futile to attempt accuracy greater than 0.10 log unit. The precision of measurement is approximately the same when readings are taken at high intensity levels during the early part of dark adaptation or at lower intensities when the eye is more completely dark adapted. When numerical plots are employed, large variations and apparent differences in speed may be entirely insignificant, because when examined on a percentage basis or on a logarithmic scale these differences may be found to lie within the limits of experimental error. Because of the daily variability of dark adaptation within 0.3 log unit, it is safest to regard only variations from the normal range which exceed this amount as abnormal.

The difference between the level of the cone threshold and the level of the rod threshold is the photochromatic interval—the range in which rods function but cones cannot. It is in this intensity range that the violet test light appears colorless. Under the standard conditions which were employed, with a violet test light viewed 7 degrees temporally, the normal photochromatic interval was found (data of Hecht and Mandelbaum [9]) to vary from 2.20 to 3.15 log units, with an average of 2.65. These figures are for the normal pupil. When a fixed or artificial 2 mm. pupil is employed a correction must be made, for the cone threshold is raised 0.2 log unit less than the rod threshold. The corrected range becomes 2.00 to 2.95 log units, with the average 2.45. The round number 2.50 log units may be taken as the average photochromatic interval when a 2 mm. pupil is employed. The cone-rod transition time occurred in almost all cases in from seven to nine minutes; a few persons showed the transition as early as six minutes or as late as ten minutes. There was nothing in the dietary history, threshold levels or ophthalmoscopic observations that would classify these extreme variations as abnormal in any sense.

E. Retinal Sensitivity Contours.—Apart from a record of the course of dark adaptation, measurements of the cone and rod thresholds over different retinal areas have been found very useful. In the normal eye the rod threshold recorded with a 3 degree violet test light is highest when the field is centrally fixated, for in the 3 degree central field

relatively few rods are present. As one proceeds peripherally the threshold drops rapidly at first, then more slowly. At 20 degrees, where the retinal rod population is most dense (about one hundred and sixty thousand per square millimeter, according to Østerberg [18]), the lowest threshold is found. Cone thresholds, however, do not depend to as great an extent on the density of the cone population. In the retinal range from 20 degrees nasally to 20 degrees temporally the cone threshold of normal eyes remains constant despite the fact that the cone population varies from one hundred and forty-seven thousand per square millimeter at the fovea to about sixty-five hundred at 20 degrees. Possibly this dissimilarity between cone and rod behavior has an anatomic basis in the difference in innervation of the two types of receptor cells. The cones are innervated individually by single nerve fibers. A great many rods, on the other hand, share a single nerve fiber. The summation of impulses is more important in rod vision than in cone vision, and there is a greater dependence on the concentration of the population of rods than of cones. The great concentration of cones at the fovea serves to make possible fine degrees of visual acuity and other discriminatory functions, rather than to make the fovea more sensitive to light.

With the instrument at my disposal measurements were limited to the horizontal meridian and within 20 degrees nasal or temporal to the fixation point. A normal contour of retinal sensitivity, as measured for both rods and cones, is indicated in the inset in chart 2, where the cone and rod thresholds are plotted from 20 degrees nasally to 20 degrees temporally along the horizontal meridian. These measurements correspond to the normal dark adaptation curve B.

Sloan [19] published threshold determinations for different retinal areas along the horizontal meridian made under "photopic" and "scotopic" conditions. Her photopic measurements presumably were to record cone function. Actually, because the background was illuminated (at 0.7 millilamberts), her readings recorded not light thresholds but intensity discrimination. Under pathologic conditions with altered cone and rod thresholds her photopic intensity level had a new relation to cone and rod function. The photopic measurements then had a significance only in relation to the level of light adaptation she employed and not in distinguishing cone from rod function. There is better physiologic justification for using a red test light in the dark-adapted eye in order to get an index of cone function. Not only in dark adaptation but in all the other carefully measured retinal functions, such as

18. Østerberg, G.: Topography of the Layer of Rods and Cones in the Human Retina, Acta ophth., 1935, supp. 6, p. 1.

19. Sloan, L. L.: Instruments and Technics for the Clinical Testing of the Light Sense: III. An Apparatus for Studying Regional Differences in the Light Sense, Arch. Ophth. **22**:233 (Aug.) 1939.

intensity discrimination, visual acuity and critical fusion frequency, the data clearly show the presence of separate cone and rod function. In all cases in which an extreme red light is used only cone function can be recorded, since the rods are incapable of responding to an illumination lower than that to which the cones respond.[8]

Because of the limitations of my apparatus, my threshold measurements apply only to the central field. Sloan's instrument permits measurements all the way out to the periphery and in any meridian; this is certainly of value in cases in which peripheral retinal function is to be studied. However, much significant information can be gained from studying the sensitivity contours of the central fields.

THE PHYSIOLOGY OF DARK ADAPTATION

A. The Photochemical Theory of Vision.—Any theory of dark adaptation must be consistent with the data not only of dark adaptation but also of the other measurable retinal functions, for dark adaptation is not an isolated phenomenon but only one aspect of the photoreceptor process. The photochemical theory of vision, as elaborated today chiefly by Hecht, provides a basis on which the known retinal photoreceptor functions, including dark adaptation, may be explained. According to this theory the sensitivity of the retina at any stage of adaptation is determined by the concentration of photoreceptor substance in the cone and rod cells—visual violet or iodopsin in the cones and visual purple or rhodopsin in the rods. During an exposure to light these substances are bleached, and both the cone and the rod thresholds are elevated. As they regenerate in the dark, retinal sensitivity increases and the familiar dark adaptation curve may be obtained.

Actually light adaptation cannot be considered in a static sense as the antithesis of dark adaptation, for there is no absolute light intensity to contrast with dark. When an eye is light adapted, it has reached a state of photochemical equilibrium in which photic degeneration proceeds at a rate equal to regeneration, and these processes balance each other (Hecht's stationary state[8]). The stationary state can be attained over a wide range of light intensities. The quantitative data of intensity discrimination, critical fusion frequency and visual acuity may be derived from stationary state equations. In the dark no photic degeneration occurs; there is only regeneration, the speed of which can easily be measured. A level of light adaptation may be maintained below the cone threshold; thus rods can function alone at certain levels of light adaptation. Also, in a completely dark-adapted eye, if a light stimulus is of higher intensity than the cone threshold, both cones and rods will respond.

The similarity between the scotopic visibility curve and the absorption spectrum of visual purple (Hecht [8] and Ludvigh [20]) can mean only that the absorption of radiant energy by visual purple provides the photochemical energy which is the first step in the visual process for rod vision. The presence of visual purple in the dark-adapted retina, its absence in the light-adapted retina and its regeneration in the dark provide the obvious basis for a photochemical theory of dark adaptation. Demonstration of the regeneration of visual purple in the test tube (Kühne [21] and Hecht, Chase, Shlaer and Haig [22]) confirmed the concept of a reversible photochemical reaction. However, cone vision was not explained until the development of more sensitive physical apparatus which permitted the demonstration of the presence of a cone-photosensitive pigment (in the retina of the chick [Wald [23]] and in the retina of the frog [Chase [24]]). The new substance was shown to have spectral sensitivity similar to cone visibility.

The demonstration of the existence of visual violet, as it has been named, filled the greatest gap in the photochemical theory. Ludvigh's [25] objections were premature, because of the tremendous difficulties inherent in the problem of working with visual violet in the extremely dilute solutions in which it is obtained. The task is further complicated by its extreme photosensitivity and by the presence of much greater concentrations of visual purple. The discovery of the cone-photosensitive pigment is of much greater importance than the objection Ludvigh made. Visual violet is probably not one substance like visual purple but three separate substances with slightly different spectral sensibilities the average sensitivity of which corresponds to the photopic visibility curve. As Hecht [26] has pointed out, only slight differences suffice to fulfil the requirements for a theory of color vision. Furthermore, in order to fit all the known data, particularly the data concerning the saturation of spectral colors, the differences must necessarily be slight. A molecular

20. Ludvigh, E.: Determination and Significance of the Scotopic Retinal Visibility Curve, Arch. Ophth. **20**:713 (Nov.) 1938.

21. Kühne, W.: On the Photochemistry of the Retina and on Visual Purple, translated from the German, London, Macmillan & Co., 1878.

22. Hecht, S.; Chase, A. M.; Shlaer, S., and Haig, C.: The Regeneration of Visual Purple in Solution, Science **84**:331, 1936.

23. Wald, G.: Photo-Labile Pigments of the Chicken Retina, Nature, London **140**:545, 1937.

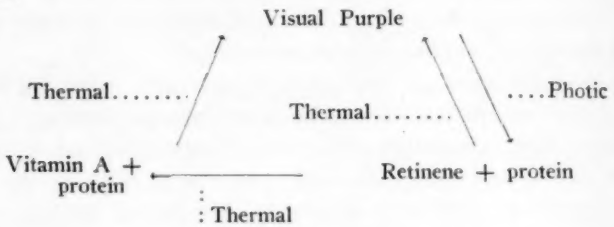
24. Chase, A. M.: Photosensitive Pigments from the Retina of the Frog, Science **87**:238, 1938.

25. Ludvigh, E.: Determination and Significance of Photopic Retinal Visibility Curve, Arch. Ophth. **24**:168 (July) 1940.

26. Hecht, S.: The Development of Thomas Young's Theory of Color Vision, J. Optic. Soc. America **20**:231, 1930.

rearrangement or the addition of a methyl or ethyl group to the molecule could easily account for the differences.

Wald [27] has shown more precisely the chemical changes involved in the bleaching and regeneration processes. Visual purple, a heavy protein molecule with vitamin A attached as a prosthetic group (Hecht and Pickels [28]), is broken down by the action of light. A new carotenoid, retinene, is liberated. This is the visual yellow stage described by early investigators. The reaction is reversible, and visual purple can be regenerated; the presence of light is not required for the reverse reaction. Retinene may be converted further to vitamin A, which by a slower process is again converted to visual purple. The following diagram, according to data reported by Wald, summarizes the process:



Dark adaptation according to classic photochemical concepts reflects simply the regeneration of the photosensitive pigments in the rod and cone cells; it is purely a retinal phenomenon and is confined to the sentient cells. This view is not universally accepted today. Although the bleaching and regeneration of visual purple are so easily demonstrated and so obviously a part of the visual mechanism, some assign it to a secondary position; others supplement this mechanism with various hypothetic nerve mechanisms, all of which are vague and for which there is no evidence.

Electroretinography provides proof that dark adaptation occurs in the retina and not in the cerebrum. After the exposure of the retina to a bright light, it requires a flash of high intensity in order to stimulate a nervous impulse, as recorded by electrical means. As the retina becomes dark adapted, the threshold brightness for the production of an impulse falls (Riggs [29]). Hartline [30] showed that in the eye of

27. Wald, G.: Carotenoids and the Visual Cycle, J. Gen. Physiol. **19**:351, 1935.

28. Hecht, S., and Pickels, E. G.: The Sedimentation Constant of Visual Purple, Proc. Nat. Acad. Sc. **24**:172, 1938.

29. Riggs, L. A.: Dark Adaptation in the Frog Eye as Determined by the Electrical Response of the Retina, J. Cell. & Comp. Physiol. **9**:491, 1937.

30. Hartline, H. K.: Dark Adaptation in Limulus, J. Gen. Physiol. **13**:379, 1930.

Limulus (a genus of crabs) dark adaptation occurred according to a chemical reaction of the second order, this being entirely consistent with photochemical concepts. Wrede [31] (using the eye of a frog) showed that the increase in electrical potential as produced by a stimulus of constant intensity during dark adaptation showed two portions, corresponding to a cone and a rod mechanism. All of these data, recording electrically impulses occurring in the optic neurons, prove conclusively that adaptation is a peripheral retinal phenomenon.

Elsberg and Spotnitz [32] arrived at other conclusions. They attempted to remove the adaptive process from the photochemical level and to deal with it on the neural level by making an analogy between the "relative refractory period" of the eye during dark adaptation and the refractory period obtained in muscles and nerves. They concluded that cerebral activity is concerned in dark adaptation, citing as evidence their ability to alter the state of the adaptation of one eye by the exposure of the other eye to bright or to dim lights. This is really a crucial point. If dark adaptation is controlled directly or indirectly by cerebral activity, the sensitivity of one eye would be influenced by the state of adaptation of the other eye.

Granit,[33] in his experiments on the electrical response of the eyes of the cat and the frog during dark adaptation, observed that the electrical response lagged behind the regeneration of visual purple. He concluded that dark adaptation could not be explained by the regeneration of visual purple alone but that intermediate factors too were of importance in the adaptive process. However, his technic for the extraction of visual purple failed to take precautions against the regeneration which occurs spontaneously in solution; therefore, the quantitative aspects of his experiment and the conclusions drawn from them are invalid.

Lythgoe [34] has leveled criticisms at the photochemical theory, maintaining that neural factors too are concerned in dark adaptation. He has also questioned the validity of the duplicity theory of cone and rod function as it is reflected in the various retinal function data that show two separate curves. Among his arguments is the fact that the cone

31. Wrede, C. M.: Time-Course of Dark-Adaptation in Frog's Eye as Revealed by Changes in Electroretinogram, Skandinav. Arch. f. Physiol. **77**:93, 1937.

32. Elsberg, C. A., and Spotnitz, H.: The Neural Components of Light and Dark Adaptation, Bull. Neurol. Inst. New York **7**:148, 1938; The Relative Refractory Period of Olfaction and Vision, ibid. **7**:78, 1938.

33. Granit, R.; Munsterhjelm, A., and Zewi, M.: The Relation Between Concentration of Visual Purple and Retinal Sensitivity to Light During Dark Adaptation, J. Physiol. **96**:31, 1939.

34. Lythgoe, R. J.: Mechanism of Dark Adaptation, Brit. J. Ophth. **24**:21, 1940.

threshold according to dark adaptation measurements is at a much lower level than the usual transition point between "photopic" and "scotopic" vision. Here, however, one is dealing with a special condition. The duplicity theory does not demand that a sharp transition point must occur between cone and rod function at the same intensity level for all functions studied. Normally there is a region of overlap, where both cones and rods function. During dark adaptation, however, a special situation is present, because the rods take a much longer time to adapt than the cones do; therefore, pure cone function can be demonstrated in the region immediately above the cone threshold, where rod function ordinarily dominates the picture. That there is such a range in which both cones and rods function simultaneously is easily demonstrable. If a violet light is viewed 7 degrees peripherally at an illumination about 0.5 log unit above the cone threshold, it appears to be pale. If, however, the eye is first exposed to the usual adapting light and the violet light is viewed after dark adaptation has progressed sufficiently to make it visible but before rod adaptation has commenced (about three minutes would be the correct time), it will appear as a saturated violet. In the first case, both the cones with chromatic vision and the rods with achromatic vision viewed the light; an unsaturated color sensation resulted from the mixture. In the second case, in the absence of the achromatic component, the color sensation was saturated. The ability of rods to function at intensity levels much higher than the cone threshold is unmistakably shown in completely color-blind persons, in whom there is no trace of cone function.

Lythgoe also cited Granit's data, despite their invalidity. Another objection he offered to the photochemical interpretation is that dark adaptation curves do not "retrace paths"; that is, from a given threshold value the course of dark adaptation is not necessarily the same but may vary depending on the previous adaptation conditions of the eye. In a simple chemical reaction the course would be the same. However, the regeneration of visual purple is not a simple chemical reaction. Wald showed that there are at least two manners in which the regeneration may take place: directly from retinene in a relatively rapid manner or by a slower route through vitamin A. The brightness and duration of the adapting light may determine which of these reactions will predominate. Dark adaptation curves of intermediate speed are the component curves of these two reactions.

Lythgoe objected to the relegation of rods to function only under conditions of poor illumination because of their great numbers in the retina. Since photopic vision is so much more important than scotopic vision, it seems a waste that so much of the retina should be occupied by rods. He neglected the phylogenetic importance of scotopic vision

and also the obvious explanation that it requires very many more sentient cells and a very much greater concentration of photosensitive pigment to function under illuminations of less than one millionth of a foot-candle, which the eye is capable of doing.

Because of his numerous objections to the photochemical theory, Lythgoe postulated that a part at least of the dark adaptation process is neural—that the rods and cones acquire progressively more fibers in common during dark adaptation, thereby increasing their sensitivity.

B. Experimental Investigation.—Two series of experiments were undertaken in order to cast some light on the process of dark adaptation. Since so many writers have considered the possibility that there is a neural component in dark adaptation, it was thought desirable to determine, first, whether the state of adaptation of one eye could be influenced by the adaptation of the second eye and, secondly, whether neurotropic drugs had any influence on the course of dark adaptation.

1. The Independence of the Two Eyes in Adaptation: I was not able to produce any measurable effect on the state of adaptation of one eye by exposing the other eye to bright light. In chart 3 the curve through the open circles shows the course of dark adaptation of the right eye as observed through a 2 mm. artificial pupil. The adapting light was 6,000 millilamberts (60,000 photons); the technic previously described was employed. The filled-in circles are readings given during a second dark adaptation test, performed under identical conditions except that the left eye was frequently exposed to a light of 6,000 millilamberts for thirty seconds during the period of dark adaptation, as indicated by the black marks on the graph. It can be seen that the filled-in circles fall along the previous curve and that no significant effect was achieved on the course of dark adaptation. In another experiment the right eye was dark adapted until the curve had flattened out at rod threshold. The left eye was then exposed to a brightness of 6,000 millilamberts for three minutes; this failed to raise at all the thresholds of the right eye, which was dark adapted. It is interesting to point out that the light to which the left eye was exposed for three minutes was two hundred million times brighter than the threshold intensity still perceived by the right eye. Not even the presence of annoying afterimages had a significant influence.

These results are entirely inconsistent with the theory of Elsberg and Spotnitz or with any theory that places importance on cerebral factors in dark adaptation. The decussation of optic fibers at the chiasma and their close intermingling in the cerebral tract and centers make it difficult to conceive of a cerebral mechanism that would allow the complete independence of the two eyes in regard to dark adaptation.

The results are, however, consistent with the photochemical theory. Wright and Nelson [35] constructed an elaborate apparatus for the recording of dark adaptation on a theory depending on the independence of the two eyes in regard to adaptation.

2. The Effect of Neurotropic Drugs on Dark Adaptation: Practically all the pharmacologic work reported in the literature is included in the review of Dorothy Adams.[36] Strychnine seems to have been the most popular drug for experimentation. Early investigators reported that after either conjunctival instillation or subcutaneous injection of this drug there was a lowering of the chromatic threshold, with an acceleration of the whole course of adaptation and a lowering of the final threshold. However, all the early work was performed on apparatus

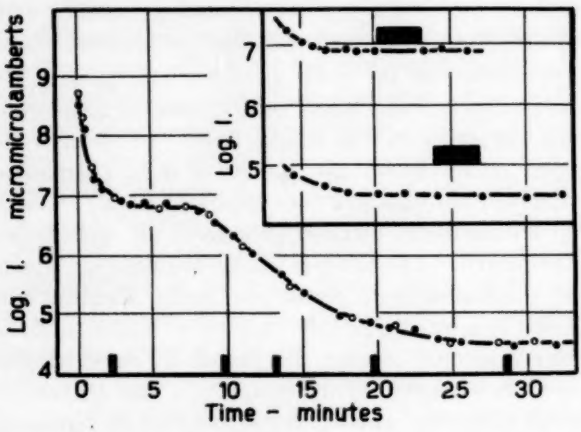


Chart 3.—The independence of the two eyes in regard to dark adaptation and threshold measurements. The determinations were made with the right eye while the left eye was frequently exposed to light, as indicated by the black marks.

which did not fulfil the known requirements for accurate measurements, and the actual adaptation curves were plotted numerically, showed irregularities and failed to demonstrate duplicity of function.

Experiments were performed according to the standard procedure as outlined in the first part of this paper. A 2 mm. artificial pupil was used; the light adaptation was to an intensity of 6,000 millilamberts. All experiments were performed on 2 trained observers. In the case of strychnine, several experiments were repeated. As much as 5 mg. of strychnine sulfate was given subcutaneously and 15 drops of a 1.5

35. Wright, W. D., and Nelson, J. H.: A Subjective Photometer, J. Scient. Instruments **12**:373, 1935.

36. Adams, D.: Dark Adaptation, Medical Research Council, Special Report Series, no. 127, London, His Majesty's Stationery Office, 1929.

per cent solution by conjunctival instillation. Six typical experiments are summarized in chart 4. For strychnine, amphetamine and alcohol, tests were made with a 1 degree field as well as with a 3 degree field. It can be seen that strychnine, amphetamine, caffeine, phenobarbital and morphine in pharmacologic doses all failed to influence significantly the course of dark adaptation.

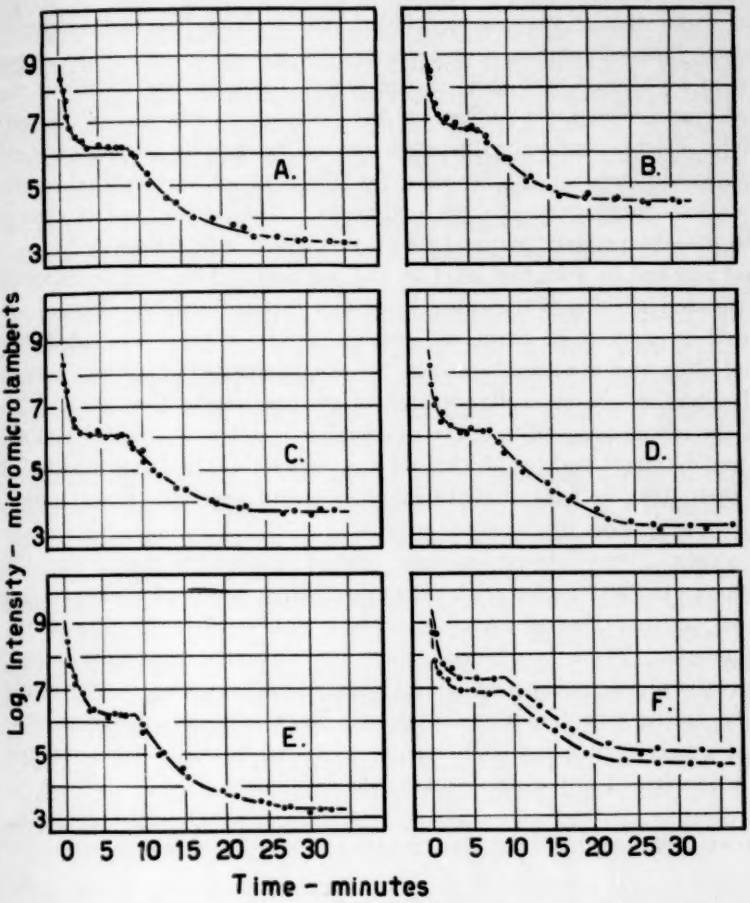


Chart 4.—The pharmacology of dark adaptation. In each case the control curve, indicated by the open circles, was followed immediately by the administration of a drug. A second dark adaptation curve was made of the same eye from thirty minutes to one hour later, when subjective and objective signs indicated that the drug had been absorbed. The data for the second dark adaptation curves are indicated by the black circles. *A*, 20 mg. of amphetamine sulfate orally, *B*, 5 mg. of strychnine sulfate subcutaneously (1 degree test light). *C*, 0.5 Gm. of caffeine with sodium benzoate subcutaneously. *D*, 20 mg. of morphine sulfate subcutaneously. *E*, 130 mg. of phenobarbital orally. *F*, alcohol orally (whisky, equivalent to 180 cc. of alcohol, and 1 degree test light).

If a neural mechanism were concerned in dark adaptation, it is most likely that an effect would have been produced through the neurotropic action of some of the drugs tried. Particularly, if the process were accompanied by changes in the neural connections of the retinal cell, as Lythgoe claimed, there would have been a decided increase in the speed of adaptation from strychnine as well as a marked effect on the final threshold levels attained.

In order that it may be concluded that a drug has had a specific effect on dark adaptation, it is necessary for the speed and shape of the curve to be altered. A shift of the whole curve up or down on the intensity axis would not suffice, for any decrease or increase in the conductivity of the conducting neurons or the receptivity of the cerebral centers could produce this nonspecific effect, in no way related to the fundamental mechanism of dark adaptation. This is the type of change I was able to produce with alcohol; the whole adaptation curve was shifted upward to a higher level by 0.3 log unit. This can be ascribed to depressed activity of the central nervous system; stronger stimuli are required in order to be perceived cerebrally. It is to be concluded that alcohol does not specifically affect the mechanism of dark adaptation. Alcohol has an action similar to that of oxygen deprivation, which also shifts the whole adaptation curve to a higher level, as shown by McFarland and Evans [37] and by McDonald and Adler.[38] The latter concluded from their data, as I do, that the effect is on the cerebral centers rather than on the process in the sentient cells.

No conclusive evidence has been offered against the theory that the two curves evident in the dark adaptation process record cone and rod function or that photochemical processes alone suffice to explain the phenomenon. There is no need, then, for elaborate hypotheses which bring cerebral mechanisms or neural phenomena occurring in the retina into the mechanism of dark adaptation. Dark adaptation may be considered a purely chemical phenomenon mediated in the sentient rod and cone cells without any extraneous neural influences.

CLINICAL APPLICATIONS OF THE MEASUREMENT OF DARK ADAPTATION

In this section I present first a summary of the present status of the relation between dark adaptation and vitamin A nutrition and then clinical data obtained in cases of various ophthalmologic diseases. No intensive review of the literature will be made; thorough reviews were published in 1929 by Adams [36] and in 1939 by Sloan.[18]

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37. McFarland, R. A., and Evans, J. N.: Alterations in Dark Adaptation Under Reduced Oxygen Tensions, Am. J. Physiol. **127**:37, 1939.

38. McDonald, R., and Adler, F. H.: Effects of Anoxemia on Normal and Vitamin A Deficient Eyes, Arch. Ophth. **22**:980 (Dec.) 1939.

A. Vitamin A Deficiency.—The early work of Fridericia and Holm [39] and of Tansley [40] pointed out that dietary night blindness was due to a deficiency of vitamin A and that more specifically the insufficient regeneration of visual purple was responsible. More recently Wald [27] showed just how vitamin A enters into the cycle of the bleaching and regeneration of visual purple. A schematic representation of the process, based on his, is reproduced earlier in this paper. To Jeans and Zentmire [41] goes much of the credit for arousing interest in this country in methods of detecting subclinical vitamin A deficiency by means of dark adaptation. Unfortunately the technic they introduced, which has become very popular because of its apparent simplicity, is subject to a great many of the errors discussed in the first part of this paper and does not give a reliable picture of dark adaptation. The method has been criticized by Hecht; the statistical validity of results obtained with it has been questioned by Palmer and Blumberg,[42] Isaacs, Jung and Ivy [43] and other investigators. Greatest emphasis is placed on the first reading obtained during the early moments of dark adaptation. As previously pointed out, this reading is unreliable because of the rapidity with which dark adaptation is proceeding during the first minutes. Furthermore, even in subjects known to be deficient in vitamin A through a deficient diet, the first readings obtained may differ but slightly if at all from normal readings. In chart 5 are shown two dark adaptation curves given by the same subject. The lower curve was obtained with the patient on a normal diet; the upper curve was obtained after the patient had been on a vitamin A–deficient diet for five weeks. It can be seen readily that the early readings practically overlap and that a much better criterion for the progress of the deficiency is the final rod threshold as given at the end of thirty minutes' adaptation. In the inset are shown the contours of retinal sensitivity as measured for both violet and red light before and after the deficient diet was begun. Apart from an elevation of the cone and the rod curves, the contour remains normal in the vitamin A–deficient state. The photochromatic interval, as indicated by the separation between the curves, is shorter because the rod threshold rises more during vitamin A deficiency than the cone threshold.

39. Fridericia, L. S., and Holm, E.: Experimental Contribution to the Study of the Relation Between Night Blindness and Malnutrition, Am. J. Physiol. **73**:63, 1925.

40. Tansley, K.: The Regeneration of Visual Purple, Its Relation to Dark Adaptation and Night Blindness, J. Physiol. **71**:442, 1931.

41. Jeans, P. C., and Zentmire, Z.: A Clinical Method for Determining Moderate Degrees of Vitamin A Deficiency, J. A. M. A. **102**:892 (March 24) 1934.

42. Palmer, C. E., and Blumberg, H.: The Use of a Dark Adaptation Technique (Biophotometer) in the Measurement of Vitamin A Deficiency in Children, Pub. Health Rep. **52**:1403, 1937.

43. Isaacs, B. L.; Jung, F. T., and Ivy, A. C.: Vitamin A Deficiency and Dark Adaptation, J. A. M. A. **111**:777 (Aug. 27) 1938.

The dark adaptation curves given by normal persons in a good state of nutrition may show a wide distribution over a range of 1 log unit.[9] Within this range no correlation could be found between the rod threshold and the state of vitamin A nutrition, as gathered from the dietary histories of the subjects. A subject who had been taking 50,000 international units of vitamin A daily for months nevertheless gave a dark adaptation curve falling just at the upper limit of normal threshold values. Similarly, in a group of apparently normal persons, Isaacs, Jung and Ivy could find no correlation between the diet and the biophotometer reading. There are, then, other factors which determine where in the normal range the adaptation curve of a person will fall. These factors may include the availability of the protein component of

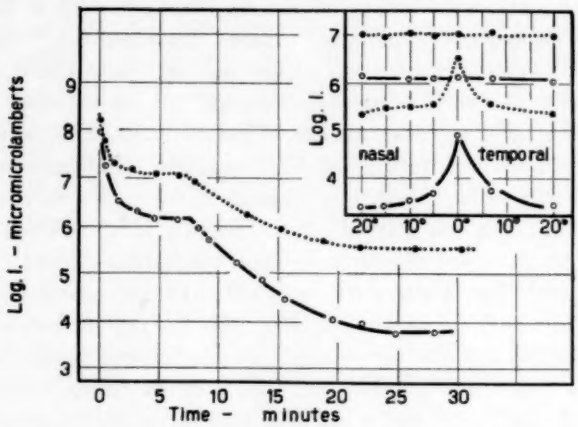

Chart 5.—Dark adaptation in experimental vitamin A deficiency. The lower curve is normal; the upper curve was given by the same subject after five weeks on a vitamin A–deficient diet. The inset shows the retinal sensitivity contours, chromatic and achromatic, corresponding to the two dark adaptation curves.

visual purple, threshold levels of the neurons in the conducting pathway or cerebral factors. Only when a dark adaptation curve is well above the normal range and no anatomic lesion can be found is it safe to say that a condition of vitamin A deficiency exists.

The response to a vitamin A–deficient diet is variable. The early experiments with vitamin-deficient diets, as reported by Hecht and Mandelbaum [9] and by Wald, Jeghers and Arminio [44] showed prompt response to the diet with very early rises in the threshold levels. However, the

44. Wald, G.; Jeghers, H., and Arminio, J.: An Experiment in Human Dietary Night Blindness, Am. J. Physiol. **123**:732, 1938.

subjects of Booher, Callison and Hewston [45] required up to one hundred and twenty-four days to show the effect. Steffens, Bair and Sheard [46] reported only very slight and insignificant changes in the adaptation of their 3 subjects, one of whom was kept on the deficient diet for six months.

The most extensive work has been reported by Hecht and Mandelbaum,[47] who have to date observed the effect of a vitamin A–deficient diet on 17 subjects. Of these, 14 subjects showed rises in the threshold of dark adaptation which began almost immediately after the commencement of the diet. The remaining 3 subjects failed to show any significant and consistent change until twenty-two, fifty-five and sixty days had elapsed. In each of the subjects showing the delayed response, the threshold began to rise rapidly and unmistakably at the end of the latent period. It is probable that the rapidity with which the thresholds rise during the deficient diet is an index to the status of vitamin A reserve of the subjects. The storage of vitamin A is apparently not related to the amount recently ingested but is more intimately connected with as yet undefined metabolic capacities which differ among persons.

In 9 subjects the recovery from the state of vitamin A deficiency as measured by the improvement in dark adaptation was studied. In no case did immediate recovery follow a single large dose of vitamin A, as has been reported by Wald, Jeghers and Arminio.[44] A measurable response was present in most cases, apparent within a few hours. In no case was the threshold lowered to normal. Nor was the drop in threshold maintained; by the next day it was back to its previous level. It was a matter of weeks and months after the return to a normal diet before normal dark adaptation could be attained. This was true even when the normal diet was supplemented with large doses of vitamin A. The presence or absence of supplementary doses of vitamin B_1, C, D and G either during the deficiency diet or during the recovery period seemed to make no difference.

It is appropriate here to mention the work of Haig, Hecht and Patek [48] and of Patek and Haig [49] with patients with cirrhosis of the liver.

45. Booher, L. E.; Callison, E. C., and Hewstone, E. M.: An Experimental Determination of the Minimum Vitamin A Requirements of Normal Adults, J. Nutrition **17**:317, 1939.

46. Steffens, L. F.; Bair, H. L., and Sheard, C.: Photometric Measurements on Visual Adaptation in Normal Adults on Diets Deficient in Vitamin A, Proc. Staff Meet., Mayo Clin. **14**:698, 1939.

47. Hecht, S., and Mandelbaum, J.: Dark Adaptation and Experimental Human Vitamin A Deficiency, Am. J. Physiol. **130**:651, 1940.

48. Haig, C.; Hecht, S., and Patek, A. J.: Vitamin A and Rod-Cone Dark Adaptation in Cirrhosis of the Liver, Science **87**:534, 1938.

49. Patek, A. J., and Haig, C.: The Occurrence of Abnormal Dark Adaptation and Its Relation to Vitamin A Metabolism in Patients with Cirrhosis of the Liver, J. Clin. Investigation **18**:609, 1939.

Because of the disturbance in hepatic function, the metabolism of vitamin A is interfered with. The change these authors observed was chiefly in the speed of the adaptation curves: there was a marked delay in the

TABLE 1.—*Dark Adaptation and Retinal Sensitivity Contours in Retinitis Pigmentosa (All Threshold Values Given in Log Micromicrolamberts in Terms of a 2 mm. Pupil)*

		Dark Adaptation (Violet Test Light in a 3 Degree Field Viewed 7 Degrees Temporally)				Retinal Sensitivity Contour (Light Thresholds Along Horizontal Meridian; Violet Test Light)							
Patient	Eye	Cone Threshold	Cone-Rod Transition Time, Minutes	Rod Threshold	Photochromatic Interval	20 Degrees Temporal	7 Degrees Temporal	Central	5 Degrees Nasal	7 Degrees Nasal	10 Degrees Nasal	15 Degrees Nasal	20 Degrees Nasal
1. H. A.*	Right	9.50	—	—	0	11.50	9.50	8.45	9.80	.....	9.85	10.55	12.05
	Left	9.85	—	—	0	12.30	9.85	8.95	....	10.55	....	.....	12.00
2. J. A.	Left	9.40	7.5	8.50	0.90	11.00	8.50	8.00	8.30	.....	9.00	9.60	11.20
3. D. B.†	Right	7.00	—	—	0	6.80	7.00	7.40	7.00	.....	7.00	7.00	6.80
4. D. Ba.	Right	7.80	7.0	7.25	0.55	9.60	7.25	6.45	....	7.25	....	....	9.70
5. S. B.	Right	9.05	—	—	0	9.30	9.05	7.05	....	8.95	....	....	9.90
	Left	8.25	—	—	0	9.10	8.25	6.95	....	8.00	....	....	9.55
6. F. F.‡	Right	9.60	—	—	0	....	....	9.60	....	....	....	....	....
	Left	8.50	—	—	0	....	....	8.50	....	....	....	....	....
7. P. F.*	Right	10.55	—	—	0	12.15	10.55	9.65	10.60	....	11.70	12.15	12.20
	Left	10.75	—	—	0	12.15	10.75	8.95	9.20	10.10	.....	11.40	11.70
8. M. H.	Right	6.60	8.2	4.50	2.10	6.90	4.50	6.00	4.60	.....	6.90	6.95	7.00
9. J. M.*‡	Right	8.70	—	—	0	10.35	10.15	8.70	....	10.50	....	....	11.30
10. B. S.	Left	8.25	9.8	7.25	1.00	8.65	7.25	8.40	....	8.10	....	....	9.10
11. B. Sl.‡	Right	7.80	—	—	0	10.20	8.40	7.80	8.50	....	9.15	9.90	10.20
	Left	7.85	—	—	0	10.15	8.95	7.85	8.75	....	9.25	9.80	10.20
12. J. S.*	Right	9.85	—	—	0	12.50	9.85	8.25	9.25	....	10.65	11.90	12.60
	Left	9.80	—	—	0	12.55	9.80	8.35	9.20	....	11.00	12.20	12.55
13. A. S.	Right	7.80	8.4	7.10	0.70	7.65	7.10	7.10	....	6.95	....	....	6.85
	Left	7.30	8.5	6.70	0.60	7.50	6.70	7.25	....	6.90	....	....	7.50
14. H. S.	Right	7.00	—	—	0	7.00	7.00	7.30	....	7.10	....	....	7.50
	Left	7.20	—	—	0	7.70	7.20	7.20	....	7.00	....	....	8.10
15. L. W.*	Right	9.90	—	—	0	9.25	9.90	7.40	9.40	....	10.40	9.20	8.95
	Left	8.75	—	—	0	8.55	8.75	7.40	....	9.20	....	....	8.40
16. L. C.	Right	8.10	7.0	7.25	0.85	9.35	7.25	6.85	6.00	....	6.00	7.90	8.55
	Left	7.90	7.4	7.15	0.75	8.50	7.15	7.00	6.30	....	6.10	7.75	8.65
17. M. W.	Right	7.60	6.2	5.80	1.80								
	Left	7.70	6.4	6.00	1.70								

* White test light.
† Retinitis punctata albescens.
‡ Dark adaptation at central fixation.

transition time between cone and rod function. This is consistent with and to be expected from the photochemical theory of dark adaptation, altered metabolic factors changing the course of chemical regeneration. Similarly, disturbances in dark adaptation which have been observed in cases of renal lithiasis [50] are undoubtedly metabolic in origin.

50. Ezickson, W. J., and Feldman, J. B.: Signs of Vitamin A Deficiency in the Eye Correlated with Urinary Lithiasis, J. A. M. A. **109**:1706 (Nov. 20) 1937.

B. Retinitis Pigmentosa.—Most of the published data on dark adaptation in patients with retinitis pigmentosa and other retinal diseases have failed to distinguish cone and rod function or to localize carefully retinal areas for study. In general, the shortcomings of the measurements have been those described in the first section of this paper.

Seventeen patients with retinitis pigmentosa (including 1 with retinitis punctata albescens) were studied in regard to dark adaptation during eighteen months at Bellevue Hospital. Many of them were examined on several occasions; because of the carefully controlled technic employed it is an easy matter even for clinic patients to give readings that are readily corroborated at a subsequent trial. The results of the

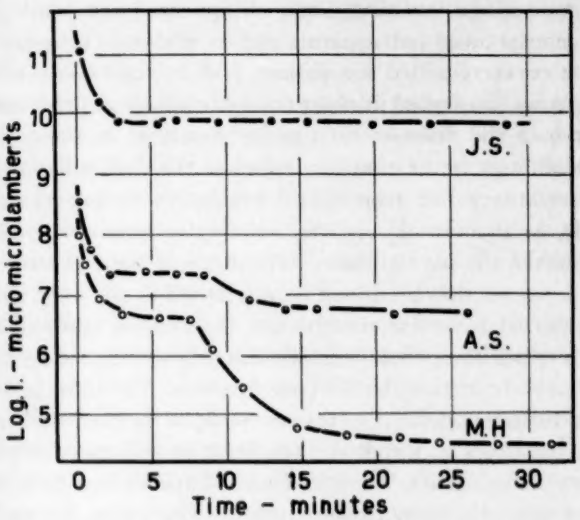

Chart 6.—Dark adaptation in retinitis pigmentosa. *M. H.* (case 8), a youth aged 18, was known to have typical retinitis pigmentosa for five years. His corrected vision was 20/30 for each eye. Perimetric examination (3 mm. test object at 250 mm.) showed ring scotomas extending from 15 to 30 degrees nasally and from 20 to 50 degrees temporally. *A. S.* (case 13), a boy aged 12 years, had a history of moderate night blindness and a family history of retinitis pigmentosa. His corrected vision was 20/70 for the right eye and 20/40 for the left eye. Perimetric examination (3 mm. test object at 250 mm.) gave normal results. Tangent screen examination (2 mm. test object at 1 meter) showed concentric contraction to about 15 degrees in each eye. Examination of the fundus revealed no pigmentation; the retinal vessels were narrow. The diagnosis was based on the typical dark adaptation changes and the family history: retinitis pigmentosa sine pigmento. *J. S.* (case 12), a man aged 45, had typical retinitis pigmentosa for sixteen years. His corrected vision was 16/70 for the right eye and 16/100 for the left eye. Tangent screen examination (10 mm. test object at 1 meter) showed concentric constriction in each eye to about 5 degrees. Measurements were made with a white test light.

studies on these patients are summarized in table 1. Typical dark adaptation curves obtained are reproduced in chart 6.

The most striking feature observed in these studies is the contraction and disappearance of the photochromatic interval. Of the 17 patients listed in table 1, a normal photochromatic interval in the retinal area studied (7 degrees temporal) is recorded for only 1 (case 8); the interval between the cone and rod thresholds was 2.10 log units. The data for this patient (M. H.) are plotted in chart 6. It can be seen that his dark adaptation curve just fell within the normal range. Six patients showed contracted photochromatic intervals which varied from 1.8 to 0.55 log unit. These curves are typified by the curve obtained for patient A. S., also reproduced in chart 6. Finally, in 10 patients the photochromatic range had completely disappeared; the dark adaptation curve no longer showed two separate curves with two separate threshold levels. The curve obtained for patient J. S. (chart 6) is of this type. The three curves illustrated in chart 6 may be taken as progressive stages in the course of the disease. It can be seen that in these there is no fundamental change in the shape or speed of the dark adaptation curves. When the secondary rod drop is still evident, it commences during the normal time, as in normal subjects. Both the cone curve and the rod curve level out in the normal time. The slope of the rod curve given by patient A. S. seems slow; this can be attributed to the very short photochromatic interval. Similar changes are observed in cases of vitamin A deficiency in which the photochromatic interval is reduced by the greater impairment of rod function than of cone function. The same general physical-chemical formulas pertain to this curve as to normal dark adaptation curves. In the cases in which the condition is still more advanced and no secondary drop occurs, the speed and shape of the dark adaptation curves correspond to normal cone curves. The curve for patient J. S. in chart 6 levels out in from three to four minutes, which is typical of a normal cone curve. There is no slow, protracted dark adaptation, but simply the elevation of a normally shaped cone curve to a higher intensity level. It is incorrect to speak of dark adaptation as being slow in retinitis pigmentosa.

In 5 cases, as indicated in table 1, dark adaptation was measured with white light rather than with violet light. In these cases the interposition of the violet filter would have made it necessary to employ a brighter light source in the apparatus, so marked were the threshold elevations. It is of course incorrect to speak of a "photochromatic interval" when the test light is white. The phrase is used, however, to define the range of intensity between the cone threshold and the rod threshold. The secondary rod curve is readily demonstrable in normal subjects with a white light as well as with a violet light. In all of these cases, however, only the primary cone curve occurred, so that the photochromatic interval was 0.

In 3 cases, also indicated in table 1, the dark adaptation test was performed with a 3 degree centrally fixated field. None of these patients showed a photochromatic interval (the average normal photochromatic interval for a 3 degree central field is 1.5 log unit).

The use of a technic for measuring dark adaptation which distinguishes between cone and rod function allows an insight into the pathogenesis of the disease. Rod function is diminished to a much greater extent than cone function, so that in moderately advanced conditions no sign of rod function may be found. The seat of a disease which has this differential effect on the function of the two types of sentient cells is most likely to occur in the bacillary layer, where the cells are discrete morphologically. In the other retinal layers the conducting neurons have more and more in common and would be less likely to be affected differentially. This confirms the actual pathologic evidence that the disease affects first the rod and cone layer. The greater functional susceptibility of the rod cells may have a real pathologic basis; possibly the greater diminution in rod function is due to the fact that rod impulses are summated much more than cone impulses and that therefore a diminution in the population of rod cells might render ineffective the summation process, discrete cones still being able to function singly.

The maintenance of the normal shape of the dark adaptation curve shows that even in advanced stages of the disease the same photochemical reactions take place as in a normal eye and at the same velocities. The shift of the curves to a higher intensity level reflects the impairment of the sentient rod and cone cells in which the adaptation occurs.

Light threshold determinations were made on these patients at different retinal areas after they had become dark adapted. As in the dark adaptation measurements, the test light was 3 degrees in diameter. Measurements were confined to the horizontal meridian. In the temporal field, readings were taken at 7 and at 20 degrees; in the nasal field measurements were usually made at 5, 10, 15 and 20 degrees. The threshold for central fixation was also measured. Included in table 1 are the results obtained with a violet test light (except in the 5 cases indicated in which the light was white). When the dark adaptation curve showed a photochromatic interval, measurements were made with a red test light as well to indicate the cone threshold levels. The cone sensitivity contours obtained in these cases were not greatly contributory; in cases in which the rod curve showed impairment of function, the cone curve did too. The data for the measurements with the red test light are not included in the table. In the cases in which dark adaptation showed no photochromatic interval the thresholds for violet can be taken to indicate cone thresholds, not rod thresholds, for the slopes of the dark adaptation curves are consistent with cone adaptation and no rod function is apparent.

Typical sensitivity contours found in retinitis pigmentosa are reproduced in chart 7. Striking changes are found. The most typical contour is that given by patient J. S. There is a complete reversal of the normal sensitivity. Instead of the central region being the least sensitive, it is the most sensitive. However, the sparing of the macular region is only relative, for even here the threshold is elevated 2.0 log units above the normal range for this region. Peripherally, sensitivity falls off very rapidly so that at 20 degrees the threshold is 12.5 log micro-

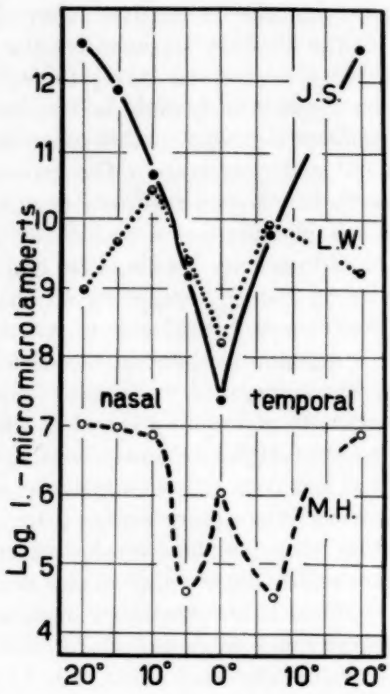

Chart 7.—Retinal sensitivity contours in retinitis pigmentosa (*M. H.* and *J. S.* described in legend of figure 6). *L. W.* (case 15), a man aged 40, a patient of Dr. B. Fread, had night blindness for five years. His corrected vision was 20/33 for each eye. There were typical retinal lesions. Perimetric examination (1 mm. test object at 330 mm.) showed asymmetric contraction varying from 3 to 22 degrees. Measurements were made with a white test light.

microlamberts, indicating for this region a diminution in sensitivity of 8.3 log units, or two hundred million times.

Ten of the 17 patients gave contour curves similar to that of patient J. S. In all these patients, routine examination of the visual fields revealed concentric contractions to small regions about the fixation point varying from 4 to 15 degrees. When the slope of the curve showing diminution in sensitivity is very steep, quantitative perimetry is of no

value whatever in establishing a gradient of retinal sensitivity. For example, patient P. F. (case 7) showed only a 5 degree field (left eye) when measured with a 5 mm. white object on a tangent screen at 1 meter. Increasing the size of the test object to 50 mm. failed to increase perceptibly the size of the field. Nevertheless, the light threshold could easily be measured out to 20 degrees, and the sensitivity gradient plotted. Similar results were obtained in the other cases.

When peripheral impairment is less marked, intermediate forms of the contour are obtained. The curve for patient L. W. (case 15) in chart 7 reveals poorest sensitivity in the region from about 7 to 10 degrees; more peripherally the sensitivity increases again. With a careful selection of test objects and illumination, a ring scotoma corresponding to this region should be demonstrable. The contour for patient M. H. (case 8) is fairly normal out to about 7 degrees; a steep diminution in sensitivity then occurs. This patient's dark adaptation curve (chart 6) fell within the normal range. The pathologic contour, however, indicates the presence of retinal pathology.

In all these cases the deviations of the retinal contours from normal indicate retinal damage of a structural rather than of a functional type. In cases of vitamin A deficiency, in which there is only a functional diminution in sensitivity, normal contours are obtained (chart 5).

A striking feature in these cases is the symmetry in the nasal and temporal regions. Only 1 patient (L. C., case 16) showed asymmetry; the nasal retina from 5 to 10 degrees was the most sensitive region. The fields showed large incomplete ring scotomas, widest in the temporal regions and avoiding the horizontal meridian in the nasal region until well out in the periphery. The relative sparing of the foveal region and the symmetry of functional impairment peripherally are typical of the changes in the retinal sensitivity contour obtained in retinitis pigmentosa.

C. Glaucoma.—Changes in dark adaptation in glaucoma have been reported by numerous observers.[51] In well advanced glaucoma, marked elevation of the light threshold occurs, as well as a diminution in all the measurable retinal functions. Early changes affecting both the speed of dark adaptation and the light threshold levels attained were reported by Waite, Derby and Kirk,[52] in 1925; they attributed important diagnostic significance to their observations. However, Casten and Shaad,[53] in a review of over 400 cases, concluded that changes in dark adaptation were not constant and were of no great diagnostic importance.

51. Sloan.[13] Adams.[36]

52. Waite, J. H.; Derby, G. S., and Kirk, E. B.: The Light Sense in Early Glaucoma, Tr. Ophth. Soc. U. Kingdom **45**:501, 1925.

53. Casten, V., and Shaad, D. J.: Diagnostic Value of Tests of the Light Sense in Early Glaucoma, Arch. Ophth. **9**:52 (Jan.) 1933.

Dark adaptation tests were performed on 24 patients with well established clinical glaucoma. When data on two eyes are given for a patient, the eye less affected had already exhibited glaucomatous manifestations, as evidenced by field changes, tonometric studies or

TABLE 2.—*Dark Adaptation and Retinal Sensitivity Contours in Glaucoma (All Threshold Values Given in Log Micromicrolamberts in Terms of a 2 mm. Pupil)*

		Dark Adaptation (Violet Test Light in a 3 Degree Field Viewed 7 Degrees Temporally)				Retinal Sensitivity Contour (Light Thresholds Along Horizontal Meridian; Violet Test Light)				
Patient	Eye	Cone Threshold	Cone-Rod Transition Time, Minutes	Rod Threshold	Photochromatic Interval	20 Degrees Temporal	7 Degrees Temporal	Central	7 Degrees Nasal	20 Degrees Nasal
1. M. B.	Right*	7.30	8.4	6.10	1.20					
	Right†‡	7.10	8.0	4.50	2.60	4.50	4.50	6.10	3.40	3.10
	Left	5.90	8.0	3.50	2.40	3.40	3.50	5.00	3.80	3.50
2. M. Bl.	Left‡	6.40	7.2	3.75	2.65					
3. B. B.	Right	7.50	8.6	5.20	2.30	4.90	5.20	6.50	5.50	5.90
4. D. C.	Right	6.40	6.6	3.50	2.90	3.20	3.50	4.60	3.50	3.20
5. J. C.	Right	6.50	7.2	4.30	2.20	3.90	4.30	5.50	4.00	3.70
	Left‡	7.40	7.6	5.40	2.00	5.00	5.40	7.00	5.80	5.30
6. A. D.	Left	6.90	6.4	5.90	1.00	6.15	5.90	5.90	5.35	6.15
7. L. E.	Right	6.50	8.0	3.50	3.00	3.20	3.50	4.80	3.60	3.30
	Left‡	7.00	8.4	4.10	2.90	3.80	4.10	5.30	4.30	4.00
8. T. H.	Right	7.15	7.8	4.25	2.90	4.60	4.25	4.50	4.40	4.80
	Left	7.50	8.0	5.50	2.00	5.60	5.50	5.60	5.00	5.20
9. W. H.	Left	6.60	7.8	4.50	2.10	4.10	4.50	5.35	4.35	3.70
10. S. L.	Right	6.70	7.4	3.80	2.90	3.25	3.80	5.20	3.65	3.40
	Left	6.70	7.6	3.80	2.90	3.40	3.80	5.40	3.80	3.50
11. E. M.	Right	7.20	7.6	4.80	2.40	5.30	4.80	6.10	4.90	4.60
12. A. N.	Left	6.70	8.0	4.00	2.70	3.60	4.00	5.30	3.90	3.50
13. M. O.	Right	6.90	8.0	5.00	1.90	4.60	5.00	6.00	4.80	4.10
	Left	6.90	7.2	4.60	2.30	4.30	4.60	5.90	4.60	4.10
14. F. P.	Right	6.95	8.8	4.05	2.90	5.00	4.05	5.60	4.20	5.60
15. I. R.	Right‡	8.05	7.5	5.40	2.65	5.20	5.40	7.30	6.20	7.80
16. E. S.	Right	8.20								
	Left	6.80	8.2	4.10	2.70	4.20	4.10	5.20	3.80	4.40
17. J. S.	Left‡	6.70	8.6	4.50	2.20	4.00	4.50	5.40	4.65	3.70
18. R. S.	Right	6.25	6.4	4.20	2.05	4.30	4.20	5.80	4.10	4.50
	Left	7.45	8.0	5.80	1.65	5.05	5.80	8.05	8.40	9.05
19. W. S.	Left‡	7.65	8.4	5.50	2.15	5.10	5.50			
20. A. S.	Right	7.10	7.6	4.40	2.70	4.70	4.40	6.20	4.60	4.40
	Left	7.05	8.0	4.50	2.55	4.20	4.50	5.60	4.90	4.20
21. A. Sp.	Right	6.80	7.2	4.50	2.30	4.80	4.50	5.50	4.25	4.00
	Left	5.90	7.0	3.50	2.40	3.40	3.50	4.50	3.60	3.20
22. A. St.	Right	6.50	7.8	4.35	2.15	4.40	4.35	5.20	4.30	4.10
23. A. T.	Left	7.10	7.0	5.00	2.10	5.20	5.00	6.10	4.80	5.10
24. Y. W.	Right	7.30	8.4	5.40	1.90					

* During acute attack of glaucoma.
† One week later.
‡ Surgical coloboma.

ophthalmoscopic observations. The results are summarized in table 2. Unlike retinitis pigmentosa, glaucoma did not markedly affect the photochromatic interval. Of the thirty-four eyes examined, an abnormally shortened photochromatic interval was observed in only four eyes, with values ranging from 1.65 to 1.00 log unit. Of these, patient M. B. (case 1) was observed during an attack of acute glaucoma; patient A. D.

(case 6) also had high myopia with choroidal and retinal degenerative changes, and patient E. S. (case 16) had congenital glaucoma. In only 1 of these patients (R. S., case 18) was the chronic simple glaucoma uncomplicated by other factors; in this case the diminution of the photochromatic interval was not great (1.6 log units).

The speeds of the dark adaptation curves were not remarkable. In all the patients the cone-rod transition occurred between six and eight and eight-tenths minutes, well within the normal range. Both the cone and the rod curves leveled out at threshold values in the normal time. However, significant elevations in the cone threshold, the rod threshold or both were found in thirteen eyes (for the retinal area 7 degrees temporally where the dark adaptation was studied); three additional eyes showed borderline elevations.

Typical dark adaptation curves obtained from glaucomatous patients are reproduced in chart 8. Of the two curves for patient M. B., one (*1*) was taken during an episode of acute glaucoma, when the intraocular tension was 65 (Schiötz); the other (*2*) was recorded a week later after an iridectomy had been performed and the tension had dropped to 22. The rod curve was curtailed to a greater extent than the cone curve during the acute phase, with a resulting diminution in the photochromatic interval. That this change was functional and not organic is indicated by the rapid recovery one week later. The data included in the table for this patient's left eye indicate practically normal dark adaptation, despite an attack of acute glaucoma in that eye four months previously. The curve for patient I. R. is normal in shape but elevated to a higher intensity level. The retinal contour as measured for cones and for rods with red and with violet light is given in the inset. The diminution in retinal sensitivity in the nasal field, as indicated in both the cone and the rod curves, is consistent with the well pronounced nasal step recorded on perimetric examination.

Included in table 2 are the threshold measurements made with violet light at central fixation and at 7 and 20 degrees peripheral fixation. When displacements from the normal contour were evident, the cone readings showed parallel behavior; data for the cone thresholds are not included in the table. When a surgical coloboma was present, the pupil area was estimated from the dimensions of the aperture.

Ten of the sixteen eyes which showed elevated threshold levels in the retinal area studied during dark adaptation showed in addition abnormalities in the retinal contours. These took the form of elevations in the threshold nasally, as in the case of patient I. R., temporally or both. Four other eyes which showed normal dark adaptation curves gave abnormal contours.

Of the total of thirty-four eyes studied, twenty showed elevated thresholds, which either were evident in the course of dark adaptation

or became apparent only in specific retinal areas when the sensitivity contour was mapped out. Of the fourteen eyes which failed to show any abnormalities a diagnosis of glaucoma had been made on clinical evidence; two had been treated surgically, and the remaining twelve had been treated with miotics for periods ranging from one month to over five years.

D. Syphilitic Atrophy of the Optic Nerve.—Twelve patients from the syphilis clinic at Bellevue Hospital (courtesy of Dr. E. Thomas and Dr. D. Goldstein) who had early atrophy of the optic nerve were studied in regard to dark adaptation. Readings were taken in the temporal field at 7 degrees. Only 4 patients showed elevated cone or

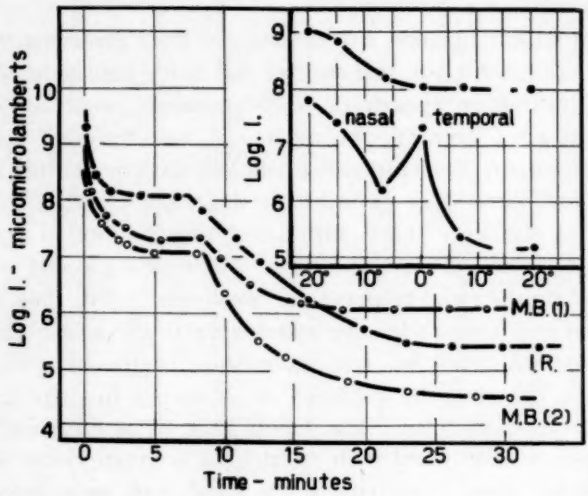

Chart 8.—Dark adaptation in glaucoma. *I. R.*, a man aged 50, had glaucoma for five years. Enucleation of the left eye was performed five years previous to the dark adaptation tests after an attack of acute glaucoma. Trephining was performed in the right eye three years previously. After that his ocular tension was controlled with miotics. Perimetric examination (3 mm. test object at 1 meter) showed a well marked nasal step, reaching to within 10 degrees of the fixation point. The inset shows the chromatic and achromatic retinal sensitivity contours for this patient. *M. B.* (case 1), a woman aged 35, had acute glaucoma. During the acute phase (*1*) tangent screen study (5 mm. test object at 1 meter) showed concentric contraction varying from 10 to 15 degrees. When the ocular tension returned to normal (*2*) the results of peripheral field examination too returned to normal.

rod thresholds; cone threshold readings as high as 7.50 log micromicrolamberts were recorded and rod readings as high as 5.60. The speed, shape and cone-rod transition times in all the curves were normal. In only 1 case was the photochromatic interval reduced (1.20 log units). Five of the patients showed abnormal sensitivity contours within the

20 degree area studied. Of these, 4 showed diminished sensitivity in the central region, as shown by elevations in both the cone and the rod thresholds, findings which are consistent with the central scotomas demonstrable in these cases. In 2 cases peripheral elevation in thresholds were demonstrable at 20 degrees.

E. Miscellaneous Conditions.—In this group are included a variety of ophthalmologic diseases which will be mentioned only briefly. Not more than a few cases were studied in any category. Two patients with toxic neuritis and central scotomas were examined; the data for one of these is reproduced in chart 9. There is moderate diminution in both cone and rod sensitivity in the retinal area where dark adaptation was tested. The cone and rod sensitivity contours showed striking rises

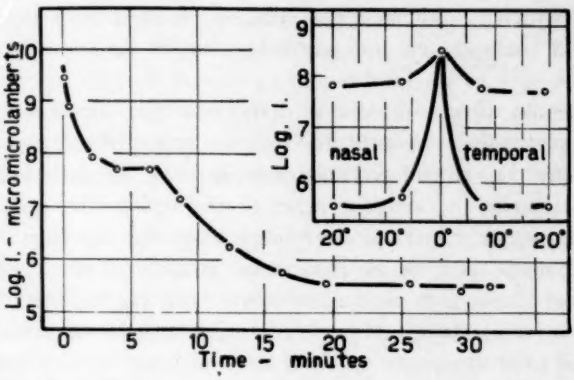

Chart 9.—Dark adaptation in toxic neuritis. A man aged 50 had had loss of vision for six months; at the time of study his visual acuity was 20/200. He drank a pint of whisky daily for fifteen years. He had also been a heavy smoker. The fundus examination gave negative results. Tangent screen examination (3 mm. test object at 1 meter) showed 3 degree central scotomas.

in the central region corresponding to the central scotoma demonstrable by perimetry. Similar but less striking contours were observed in cases of syphilitic atrophy with central scotomas.

Nothing typical was observed from a study of various types of choroidoretinopathy—hypertensive, diabetic or myopic. Elevated thresholds were recorded in cases in which pathologic changes were present. There was no alteration in the shape or speed of the dark adaptation curves in the early stages; in the late stages with choroidal involvement, high threshold elevations were recorded when pathologic retinal areas were examined, often associated with a loss of the photochromatic interval.

COMMENT

In none of the pathologic conditions studied has there been observed what can correctly be called slow dark adaptation. Only in retinitis pigmentosa was there a specific effect on the course of dark adaptation; this was not in the nature of a diminution in the speed of the adaptation curve but a selective effect on the rod curve. Rod function became increasingly impaired until it apparently disappeared completely, leaving a cone curve with normal shape and speed but at a higher intensity level. This translation to higher intensity levels, which occurred most markedly in retinitis pigmentosa but also appeared in the cases of advanced glaucoma, atrophy of the optic nerve and other diseases studied, cannot be attributed to faulty dark adaptation, for the dynamics of the process, as indicated by the maintenance of normally shaped adaptation curves, has not altered. There is rather a general diminution in retinal sensitivity, which is indicated not only by elevated light thresholds but also by field contractions and any other retinal function test that may be applied.

The unequal effects on cone and rod function which were observed in retinitis pigmentosa, as indicated by contraction of the photochromatic interval, may be considered characteristic of a pathologic process affecting primarily the sentient layer of the retina, the function of the rod cells having a greater susceptibility than the function of the cone cells. In cases of chronic glaucoma and atrophy of the optic nerve, in which retinal damage is neural in origin, the photochromatic interval remains relatively intact. However, during attacks of acute glaucoma a contracted photochromatic interval may be observed; under these circumstances it is likely that the functions of the cone and rod cells are directly affected by the high intraocular tension.

The measurement of light thresholds for different retinal areas permits for the first time a really quantitative method of retinal sensitivity topography. The limitations of quantitative perimetry in establishing a contour of retinal sensitivity have long been recognized; technics for perimetry under reduced illumination have been introduced in order further to increase the scope of perimetry. These methods not only involve lengthy procedures but also require complex theoretic analysis for interpretation. It is much simpler from a practical and from a theoretic point of view to measure directly light thresholds rather than to alter not only the size of the test objects but also the illumination. The value of this method is particularly striking when the retinal sensitivity changes at a steep rate, as for patient J. S., in chart 6. Here attempts to gage the slope of the defect by means of alterations in the size of the test object would be futile, as only a small central field is indicated regardless of the size of the test object. When "relative"

defects are indicated by quantitative perimetry, the exact extent of loss of retinal sensitivity may be measured most simply by threshold determinations.

SUMMARY

The physiologic requirements for proper dark adaptation measurements include: control of brightness and of duration of exposure to the preadapting light, retinal fixation and size and color of and duration of exposure to the test light.

The achromatic threshold, as measured with violet light, shows a direct dependence on the size of the pupil; the chromatic threshold measured with red light falls a little short of the direct proportionality curve. Correction curves for pupil size have been presented.

Various objections to the photochemical theory of dark adaptation have been discussed. The demonstration of the complete independence of the two eyes in regard to adaptation and the failure to affect significantly the course of dark adaptation by the use of various neurotropic drugs support the photochemical theory of vision.

Determinations of dark adaptation in 110 normal persons, corrected for a 2 mm. pupil, show a range in rod thresholds from 3.5 to 4.5 log micromicrolamberts; the cone thresholds range from 6.0 to 6.8 micromicrolamberts.

Normal retinal sensitivity contours both for cones and for rods have been presented. Rod sensitivity apparently depends on the rod population. The cone threshold level is the same from the fovea to 20 degrees peripherally, despite large changes in the cone population.

In vitamin A deficiency the most striking change in dark adaptation is the rise of the rod and cone thresholds. Retinal sensitivity contours remain normal in shape.

In no pathologic conditions of the eye has there been observed a specific retardation in the speed of the dark adaptation curve.

In retinitis pigmentosa the rod function is diminished to a much greater extent than the cone function. The depression of peripheral retinal sensitivity is characteristically symmetric around the fovea.

In glaucoma and atrophy of the optic nerve cone and rod function are depressed about equally. Elevated cone and rod thresholds indicate diminished retinal sensitivity; the dynamics of dark adaptation do not appear to be altered.

Plotting the figures obtained for cone and rod thresholds at different retinal areas provides for the first time a really quantitative method of retinal sensitivity topography.

RECESSION OF RETINAL PAPILLEDEMA DURING TERMINAL STAGE OF MALIGNANT HYPERTENSION

REPORT OF A CASE

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Several observers have reported recession and even disappearance of the characteristic retinitis associated with malignant hypertension. Usually the improvement in the retina has been accompanied with a period of amelioration in the general condition. In our case, however, during the progressive terminal course, three weeks before death, a previously measurable papilledema disappeared and retinal hemorrhages and exudates became less numerous. Pathologic study of the retina confirmed the absence of papilledema. It seemed pertinent, therefore, to report these facts and to endeavor to offer an explanation for them.

REPORT OF CASE

The patient was 38 years old and was the father of three healthy children. On admission to the clinic (June 12, 1939) his chief complaints were severe headaches and dimness of vision. He had been told by his local physician that his blood pressure was elevated. His family history was not significant except for the fact that his sister had hypertension. In 1929 colicky pain developed in the region of the left kidney and disappeared after left ureterolithotomy. Headaches with nausea developed in 1934, and the episodes became much more frequent in 1936. At that time his blood pressure was found to be slightly elevated, 160 mm. of mercury systolic and 90 mm. diastolic. The blood pressure rose steadily after 1936. In 1938, one year before admission to the Mayo Clinic, it was 170 mm. of mercury systolic, and three months before admission it was 230 systolic and 110 diastolic. The patient's vision began to fail six months before admission and continued to fail until he could not read. During the same period he lost approximately 30 pounds (13.6 Kg.) in weight, and some dyspnea and palpitation on exertion developed.

From the Division of Medicine (Dr. Keith), the Section on Ophthalmology (Dr. Rucker) and the Division of Surgical Pathology (Dr. Parkhill), the Mayo Clinic.

Physical Examination.—The patient's height was 67 inches (170 cm.), and he weighed 130 pounds (59 Kg.). The oral temperature was 98 F. He appeared thin, pale and nervous. There was considerable palpable thickening of the peripheral arteries. On percussion the heart was moderately enlarged; the second sounds were accentuated over the base of the heart, but no murmurs were heard. The blood pressure was 230 mm. of mercury systolic and 140 mm. diastolic. No distinct neurologic abnormalities were observed.

Ophthalmologic examination revealed that vision in the right eye was 14/56, and in the left, 14/224, as tested with the American Medical Association reading card. The poor vision in the left eye was the result of amblyopia ex anopsia. The pupils reacted promptly, and the visual fields were roughly normal; bilateral papilledema of 3 D. on the right and 2 D. on the left was present; the retinal arterioles were generally narrowed, with some moderate sclerotic changes; a few localized constrictions of the arterioles were seen, and many hemorrhages and cotton-wool exudates were present in the peripapillary regions.

Laboratory Studies.—Routine urinalysis revealed albuminuria grade 3, a few granular and hyaline casts, a few erythrocytes and no reducing constituents.

Observations on the Spinal Fluid

Date, 1939	Pressure of Spinal Fluid, Cm. of Water		Appearance	Amount Withdrawn, Cc.	Number of Cells per Cu. Mm.
	Initial	Final			
6/22	36	14	Clear	25	..
7/10	14	*	Clear	12	..
7/18	24	*	Clear	*	1

* Pressure and amount not recorded.

Examination of the blood revealed a concentration of hemoglobin of 11.6 Gm. per hundred cubic centimeters and counts of 4,090,000 erythrocytes and 7,500 leukocytes per cubic millimeter. The serologic test for syphilis gave a negative reaction. The concentration of urea and that of creatinine in the whole blood were 116 mg. and 5.4 mg. per hundred cubic centimeters respectively. The concentration of serum sulfate was 15.7 mg. per hundred cubic centimeters. The carbon dioxide–combining power of the plasma was 57.9 volumes per cent.

A roentgenogram of the thorax revealed moderate enlargement of the cardiac shadow and evidence of congestion of the lungs. A roentgenogram of the head revealed nothing abnormal. An electrocardiographic tracing indicated sinal tachycardia, with significant abnormal changes in the T wave in leads I and II.

Course in the Hospital (June 12 to August 9).—The patient's condition during this period of fifty-nine days became progressively worse. Cheyne-Stokes respiration occurred periodically, and the renal insufficiency increased. The concentration of urea and that of creatinine in the blood rose to 428 and 8.8 mg. per hundred cubic centimeters, respectively. At times the patient was mentally confused. Periodically a distinct pericardial friction rub was heard. Much to our surprise, on July 21, the thirty-ninth day after admission, examination of the ocular fundi revealed disappearance of the papilledema; the disk margins were distinct, and the nasal halves of the disks were structurally full. Hemorrhages and exudates were present. During the interval from June 14 to July 21 the blood pressure had

remained high. Four readings on the latter date varied from 195 to 200 mm. of mercury systolic and from 145 to 150 mm. diastolic. Spinal puncture was carried out on three occasions. The results are given in the table.

On August 5 there was still no edema of the disks. The blood pressure varied from 170 to 180 mm. of mercury systolic and from 110 to 130 mm. diastolic. During the last week of his illness the patient became much weaker; periods of Cheyne-Stokes respiration became more frequent, and signs of pulmonary edema were present from time to time. Death occurred on August 9.

Clinical and Pathologic Diagnoses.—The clinical diagnosis was diffuse arteriolar disease with hypertension in the malignant phase; myocardial degeneration with decompensation; pulmonary edema; pericarditis; cerebral edema; retinitis of diffuse arteriolar disease, and severe renal insufficiency.

The pathologic diagnosis was arteriolar sclerotic atrophy of the kidneys (weight 224 Gm.); hypertrophy of the heart (470 Gm.); multiple infarcts of the brain; fibrinopurulent organizing pericarditis; hydrothorax on the left side, and bronchopneumonia.

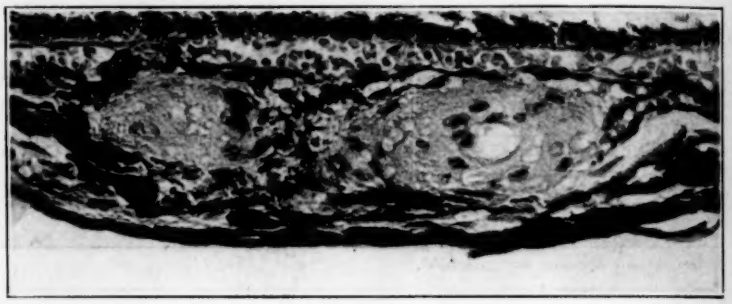

Fig. 1.—Marked thickening of the walls of the choroidal arterioles. Proliferation of the intima and hyaline thickening of the media are seen; the lumen of one arteriole appears to be completely occluded. Hematoxylin and eosin; × 350.

Pathologic examination of the right eye revealed retinitis of the hypertensive type and sclerosis of the choroidal arteries.

Microscopic Examination.—Right eye: The corneal epithelium was thinned and in places abraded. The anterior chamber was of good depth, and the filtration angle was open. There was slight hyalinization of the walls of some of the blood vessels of the iris. There was marked thickening of the walls of many of the choroidal arteries and arterioles. The most frequent and most marked changes were hyalinization of the media and proliferation of the intima, although hypertrophy and fibrosis of the media and the adventitia and perivascular fibrosis were seen. In many of the vessels the lumen was reduced markedly in caliber, and in a few it was completely obliterated (fig. 1).

In the retinal vessels the lesions were less striking. Although noticeable change was not present in many of the vessels, a number of scattered arterioles were seen with definite thickening of the wall and narrowing of the lumen, slight in some and more marked in others. In most of these vessels proliferation of

the intima and hypertrophy or hyalinization of the media were present. Although "retinitis" persisted in a few places, the retina on the whole appeared well preserved. A small area of cystic degeneration was present anteriorly, and some vacuolation was seen in the region of the ganglion cell layer, but well preserved ganglion cells could be seen throughout most of the retina. Posteriorly there were a few small areas of hemorrhage and edema. In one such area, about 4 mm. nasalward from the disk, a small hemorrhage involved chiefly the inner layers of the retina, while in the outer nuclear layer small accumulations of clear eosinophilic homogeneous "exudate" could be seen (fig. 2*a*). The arterioles in this

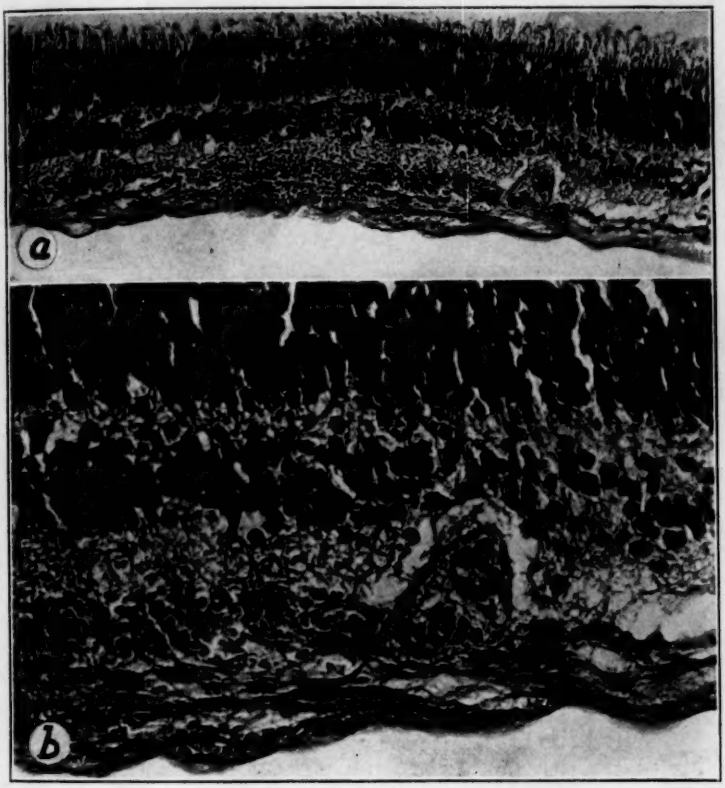

Fig. 2.—Retina. Photomicrograph *a* shows hemorrhage in the inner layers of the retina, adjacent to retinal arterioles with thickened walls. In the outer nuclear layer of the retina are masses of clear eosinophilic "exudate." Hematoxylin and eosin; × 135. Photomicrograph *b* shows the arterioles in *a* under higher magnification; thickening of the walls, proliferation of endothelial cells and almost obliterated lumens are evident. Hematoxylin and eosin; × 350.

region had thickened walls and endothelial proliferation with almost obliterated lumens (fig. 2*b*). In adjacent sections hemorrhage could be seen extending into the deeper layers of the retina, and "cytoid bodies" were present in the nerve fiber layer (fig. 3). Another small group of "cytoid bodies" was seen in the nerve fiber layer temporal to the disk, and in the region of the macula there were small accumulations of clear eosinophilic homogeneous exudate in the outer retic-

ular layer. The optic disk was flat, and there was a small physiologic cup. There was no evidence of edema in the nerve head (fig. 4). Fifty-nine days before death the ophthalmoscopic examination had revealed papilledema of 3 D.

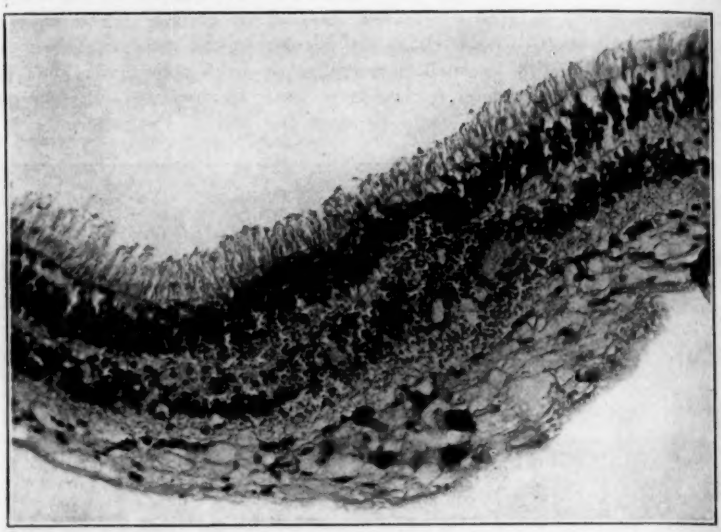

Fig. 3.—Hemorrhage in the retina extending to the outer reticular layer. Note the "cytoid bodies" in the nerve fiber layer. Hematoxylin and eosin; × 150.

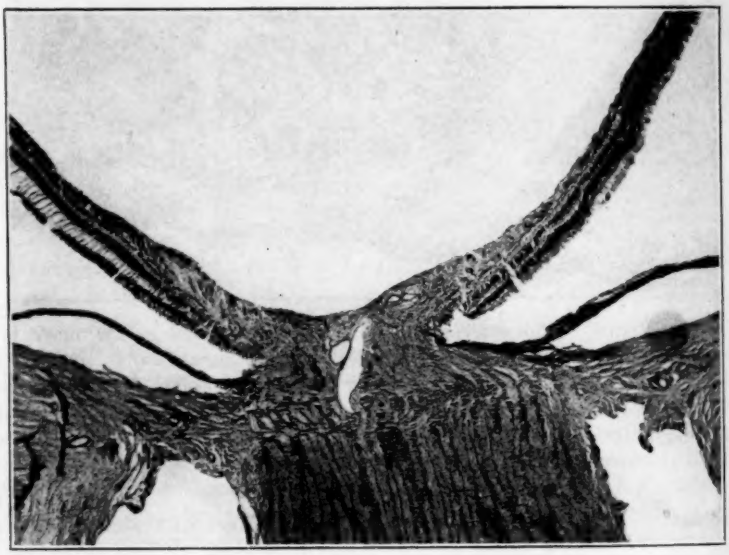

Fig. 4.—The optic disk is flat, and there is no evidence of edema. The wide lumen and thin walls of several retinal vessels can be seen. Hematoxylin and eosin; × 20.

Kidney: The changes in the smaller arteries and arterioles were strikingly similar to those in the vessels of the choroid. Intimal proliferation, hyaline thickening of the media and often marked narrowing of the lumen were prominent. In addition, the walls of the larger vessels were notably thickened, with proliferation of intima, reduplication and splitting of the tunica elastica and hypertrophy of the media. The glomeruli also were changed frequently. Some appeared practically normal; others showed alterations ranging from increase of endothelial nuclei and narrowing of the capillary lumen to complete hyalinization of the glomerulus. In addition to the perivascular fibrosis there was widespread interstitial fibrosis (moderate). Many of the convoluted tubules were dilated and contained coagulated protein, erythrocytes, leukocytes and hyaline casts (fig. 5).

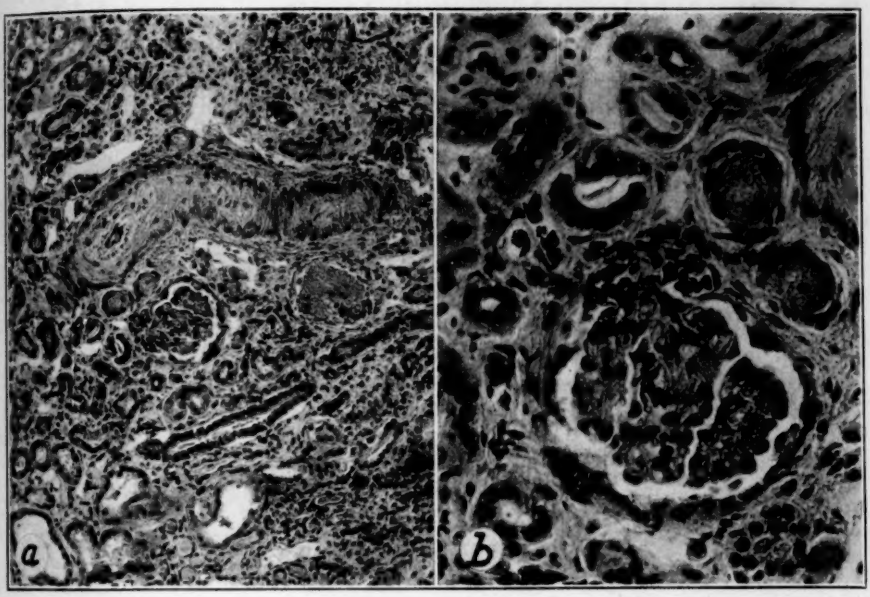

Fig. 5.—Kidney. Photomicrograph *a* shows interstitial fibrosis and sclerosis of arteries and arterioles; one glomerulus is completely hyalinized. Hematoxylin and eosin; × 100. Photomicrograph *b* shows a portion of *a* under higher magnification; marked hyaline thickening in the walls of two arterioles and almost complete obliteration of lumens may be noted. The glomerulus shows increased endothelial nuclei. Hematoxylin and eosin; × 320.

COMMENT

It has been pointed out repeatedly that the clinical course and extent of the vascular pathologic changes vary considerably in cases of malignant hypertension. In the present case subsidence of neuroretinal edema, usually associated with temporary remission of the diffuse disease, occurred nineteen days before death, when the patient was almost moribund. Indeed, during the subsequent nineteen days the diffuse vascular

process was definitely progressive elsewhere than in the retina, as was evident by the increasing dysfunction of several vital organs, especially the brain, heart and kidneys. By what biologic process was it possible for the retinal lesion, particularly the papilledema, to improve so strikingly while the function of the other organs was literally being slowly strangled? We do not believe that there is at present a simple, cleancut explanation. Spinal puncture on three occasions, with removal of a total of approximately 50 cc. of spinal fluid, scarcely seems an adequate explanation, for (1) the intraspinal fluid pressure was increased to 24 cm. of water three days before recession of papilledema was observed; (2) the recession continued for the next eighteen days, until death, and (3) spinal puncture has not noticeably reduced the papilledema in many similar cases of malignant hypertension. A possible explanation is that some compensating mechanism or mechanisms developed at this particular time in the peripheral vascular blood supply to the retina. The unequal histopathologic involvement of the retinal arterioles suggests that there may have been a sufficient number of normal arterioles present in the retina to give a blood supply adequate for reabsorption of the papilledema.

TREATMENT OF HERPETIC KERATITIS WITH ETHER

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Many remedies have been proposed for the treatment of herpetic keratitis. The medicament most widely in use is tincture of iodine. Others which have been advocated are 90 per cent alcohol, hydrogen peroxide, fresh chlorine water phenol, trichloroacetic acid, copper sulfate stick, ethylmorphine hydrochloride, mercurochrome and quinine bisulfate. This is a preliminary report on the results secured by applying anesthetic ether directly to herpetic lesions of the cornea.

As Grüter [1] established in 1920, the organism causing the herpetic lesions is a specific virus which is transmissible from man to animals. There is a relation among the various forms of herpes, i. e., herpes labialis, herpes facialis and herpes genitalis. The virus itself is an ultramicroscopic filter-passing organism. In the cornea the organism causes small grayish translucent infiltrates, which lie beneath the epithelium and elevate it. These elevations are associated with each other in irregular branching lines. They are frequently ulcerated. Microscopic sections show small foci of polymorphonuclear infiltration in the superficial layers of the corneal stroma, and over this are bleblike elevations or ulcerations of the epithelium.

Roggenkämper [2] made brief reference to 22 cases of corneal conditions which he reported merely as having been treated with ether. Eleven were cases of herpetic keratitis. He stated that in 7 the lesions healed with one application, in 3 they healed with two applications and in 1 they healed rather slowly.

This report comprises 8 cases of herpetic keratitis treated with ether. The number of applications necessary varied from one to ten, but the results obtained were uniformly good. In the cases requiring the most applications the greater part of the vesicles had completely healed with only two applications, but a few small vesicles remained unhealed. A change in the technic was made, and these lesions healed rapidly. It

Presented at the New York Society for Clinical Ophthalmology on March 3, 1941.

1. Grüter, W.: Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. (1920) **42:** 162, 1921; Klin. Monatsbl. f. Augenh. **45:**398, 1920; cited by Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2.

2. Roggenkämper: Ophthalmologica **96:**189, 1938.

was found that unless the ether was rubbed in well some of the vesicles remained open. The application of tincture of iodine was used to supplement the ether treatment in 1 case because a single vesicle remained open for a long time. In 1 case only one treatment was required; in 4 cases the lesions healed after two applications; in 2 cases three applications were required, and in 1 case ten applications plus a supplementary application of iodine were needed. There was no reaction or pain after the use of ether in any of these cases.

The method of application employed in the cases reported here was as follows:

1. Local anesthesia was obtained by the use of any of the standard local anesthetics, such as pontocaine hydrochloride, metycaine hydrochloride or larocaine hydrochloride.

2. A cotton applicator was then dipped into the ether and quickly applied to the corneal lesions. (In this procedure several mistakes can be made. To guarantee the wetness of the applicator, the container of ether must be held close to the patient. If this is not done, the rapid evaporation of the ether will result in the drying of the applicator before it touches the lesions. The lesions must be rubbed firmly with the wet applicator. Failure to use the correct technic is probably the cause of the poor results obtained in some cases.)

3. After instillation of atropine sulfate and any of the antiseptic ointments, a patch was applied.

The ether method of treating herpetic keratitis has at least two outstanding advantages over the iodine treatment commonly used today. In contrast to the extreme pain and severe reaction characteristic of the treatment with tincture of iodine, the ether treatment is absolutely painless and without reaction. At no time, either during treatment or afterward, did any of the patients complain of pain. In no case was there any conjunctival edema after treatment. Still another objection to the iodine method is that the treatment is frequently prolonged over many months. The ether treatment, on the contrary, is so rapid that in some cases the patients are considered healed within a few days.

The explanation of the specific action of ether on the virus is not definite. Ether applied in such small quantities and for so short a period certainly cannot act as a germicide. The reduction of the temperature is also unacceptable as an explanation, since the virus is cold resistant. A specific action of some sort—perhaps a chemical affinity—must therefore be assumed.

In personal conversations with me, Dr. Ernst Waldstein, of New York, reported good results in 6 cases of herpetic keratitis treated with ether. His patients also required only a small number of applications.

REPORT OF CASES

CASE 1.—L. N., a white man aged 22, complained of epiphora, photophobia and pain in the left eye caused by a small foreign body. On staining with fluorescein, a typical herpetic lesion was seen in the cornea.

On December 26 ether was applied to the lesion and a patch was put on. On December 27 the vesicles were completely healed.

Only one application of ether was required.

CASE 2.—M. M. D., a white woman aged 22, complained of pain, sensitivity to light and epiphora of three days' duration. A diagnosis of herpetic keratitis was made. Ether was applied on September 17.

On September 18 the lesion was almost completely healed, and ether was applied again. On September 19 only one small vesicle remained open. On September 21 the patient was seen again; the lesion was completely healed.

Three applications of ether were required.

SUMMARY

The use of anesthetic ether in the treatment of herpetic keratitis is reported.

The technic is described.

There is no reaction or pain following the use of ether.

The rapid and painless recovery shows this method to be a radical improvement in the treatment of herpetic keratitis.

The explanation of the action of ether has not been definitely determined. A chemical affinity is suggested.

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PATHOLOGY OF ACUTE GLAUCOMA

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According to a general physiologic and anatomic law of the vegetative nerves, the efferent fibers of this system are interrupted once in one ganglion and afterward reach their termination, in contradistinction to the cerebrospinal nerves, which run directly uninterrupted from their nuclei to their peripheral ends in the musculature (Langley[1]). This law of innervation of the inner organs shows allegedly two exceptions: 1. The two large nerve trunks of the gastrointestinal tract, the vagus nerve and the sympathetic nerve, have a first interruption in the celiac plexus and a second in the Auerbach and Meissner plexuses. 2. The fibers of the oculomotor nerve, after having found a real interruption within the ciliary ganglion, are not distributed in the smooth muscles of the eyeball but allegedly present a second synapse within the ciliary plexus. The function of the ciliary plexus, whose very rich fibers are imposing, and the importance of the so-called second interruption (this has never been conclusively demonstrated) have been disregarded by oculists. Although the following comments and considerations, which result from a prolonged study, are partially hypothetic, they deserve some consideration, because the aforementioned anatomic fact, together with a second and a third morphologic peculiarity of the eye, proves that the modern concept of the structure and function of the eye presents many gaps.

The structure of the ciliary ganglion and its relation to three roots make it different from all similar structures in the human body. Modern anatomists, particularly Stoehr, have not hesitated to ascribe to it a special position, without any analogy in the organism. It consists, according to my investigations and those of Mueller, almost exclusively of multipolar cells, such as are usually seen in sympathetic ganglions.

The fibers of the vegetative system, after having passed the synapse, are commonly not medullated. In contradistinction to this, the small ciliary nerves are medullated. Therefore, it may be doubtful whether one is dealing with a real synapse or whether the fibers of the oculomotor nerve pass through the ganglion in the same manner as do the sympathetic fibers derived from the carotid plexus, without a real inter-

* Formerly professor at the University of Vienna.

1. Langley, J. N.: J. Physiol. **39**:56, 1922. Starling, E. H.: Principles of Human Physiology, ed. 4, London, J. & A. Churchill, 1926, p. 383.

ruption. In this case Langley's general law, previously mentioned, would obtain, and the interruption of the ciliary nerves would take place within the ciliary plexus. I cannot agree with this hypothesis, because the ciliary plexus does not carry ganglion cells. On the other hand, it should not be forgotten that the number of fibers within the ciliary nerves is larger than that in all three roots of the ganglion. Certainly the reason for this could be either that the entering nerve fibers are subdivided or that some of the fibers are derived from ganglion cells of the ciliary ganglion. The majority of anatomists assume a synapse within the ganglion.

By many clinical and pharmacologic observations it has been proved that any organ is doubly innervated. This is also true of the pupils. A sympathetic innervation of the ciliary muscle, however, has never been conclusively demonstrated.[2]

ANATOMIC CONSIDERATIONS

By some investigators it has been stated that the ciliary processes are a secretory organ of the bulbus oculi. They are dominated by nerves. The secretion of the ocular fluids and their circulation within the eyeball are controlled by the ciliary plexus. This point of view is important for a concept of the pathologic picture of acute glaucoma.

It is obvious that the outflowing fluids of the eye will finally reach, as does the cerebrospinal fluid, the general venous system. Within the skull, one encounters the arachnoidal cisterns, the sinuses of the dura and the emissaria of the skull. Comparing the coverings of the eyeball with the coverings of the brain, one encounters easily within the bulbus the arachnoidal cisterns, the sheath spaces of the optic nerve, the perichoroidal space, the large anterior and posterior cameras and the openings within the pectinate ligament. The canal of Schlemm belongs to this system. Normally it carries not blood but ocular fluid. The venous plexuses surrounding the canal of Schlemm on the outer and posterior aspect are comparable to a sinus of the brain.

Besides the ciliary body and the optic apparatus, the structure of the veins, particularly of the venous plexuses of the eye, deserves attention. Wherever in the organism one encounters venous pads, plexuses or cavernous bodies, one is dealing with structures of special function. Mention may be made of the venous plexuses of the vertebral column, of the large venous plexuses within the pelvis (the veins coming back from the limbs are simple, whereas the veins of the genital organs form large plexuses) and of the venous plexuses of the nasal cavity, which present real cavernous organs.

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2. Morat, J. P., and Doyon, M.: Arch. de physiol. norm. et path. **3**:507, 1891. Heese, E.: Arch. f. d. ges. Physiol. **52**:535, 1892.

The venae vorticosae may be considered first. These veins before entering the scleral canal show remarkable dilatations, the sinus vorticosi. The walls of these veins close to the sclera are much thinner than in the neighborhood of the choroid. The same is true of their course within the sclera. Slightly proximal to their mouths they become remarkably thick, partly because of the greater development of the media and partly because of the development of longitudinal fibers. The same peculiarity, namely, the development of a special inner layer of longitudinal fibers, is to be found within the veins of the intestines, the uterus and the corpora cavernosa of the penis. The pressure within the dilated sinus vorticosi should be relatively high. This would be a counteraction against compression of the veins by the pressure of the bulbus oculi. It is possible that an increase of this pressure may produce shutting of the scleral veins. The importance of venous occlusion has been proved in the case of the adrenal veins by Maresch and in the case of the hepatic veins by Mauthner and Pick. The pressure within the intrascleral section of the veins is normally low, but the veins are protected against compression by their close connection with the tissue of the sclera. The superior ophthalmic vein sometimes shows (this fact should be carefully reexamined) a sinus-like dilatation (sinus ophthalmicus) in the lateral superior aspect of the superior orbital fissure. Before entering the cavernous sinus, it has frequently a communication with the sphenoparietal sinus. In close connection with the veins of the orbit are the following sinuses and plexuses: the sinus cavernosus; the plexus venosus caroticus; the plexus venosus pterygoideus (comunicating with the veins of the orbit by a large branch and with the sinus cavernosus by the veins of the foramen ovale, the foramen lacerum and the foramen Vesali); the sinus sphenoparietalis, and the plexus venosus nasolacrimalis.

Since the two large veins of the orbit, the superior and the inferior ophthalmic veins, do not show valves, and since it is generally not possible to state the direction of their blood flow, it is likely that the blood stream within the ophthalmic veins is dominated by nervous impulses. This seems all the more plausible since wherever there are venous sinuses or plexuses there are strong nerve trunks, nerve plexuses or numerous ganglion cells. One is reminded of the venous plexuses within the vertebral column, surrounding the spinal ganglions and the roots of the intercostal nerves; of the pudendal plexus, with its close relation to the nerve plexuses of the pelvis; of the internal carotid plexus, which is closely connected with the sympathetic nerve plexus; of the plexus venosus pterygoideus, surrounding the plexus nervosus pterygoideus of the internal maxillary artery, in the vicinity of which one finds the sphenopalatine ganglion with its fibers. It goes without saying that the aforementioned venous plexuses of the eyeball are located in the neigh-

borhood of nerve branches. Knowledge of the structure and function of the wall of the vein is incomplete. A conclusion as to the importance of the venous plexuses under discussion should be drawn carefully. It is obvious that the structure of the sinus vorticosi is adapted to mechanical purposes. The numerous nerves in the neighborhood of the venous plexuses communicating with the veins of the orbit; the lack of valves in the main veins of the eyeball, and the lack of lymph vessels within the bulbus (except for the canal of Schlemm) are noteworthy. *I suggest that there may be a neural control of the venous circulation of the bulbus which dominates its velocity and direction.* Disturbances of the venous flow are likely to be important in the pathogenesis of glaucoma. Considering the relation of the circulation and the optic nerve, which may early prove deleterious in the case of increased intracranial pressure, I incline to the opinion that an increased pressure within the bulbus in its turn may influence the circulation of the fluids within the brain and its membranes.

FUNCTION OF THE CILIARY GANGLION

Since opinions concerning the function of the ciliary ganglion are different, it is necessary to try to elucidate this problem. The fundament will be the basic anatomic and embryologic facts. It is obvious that the pharmacologic and physiologic concepts are rather confusing.

In accordance with the concept of an active migration of nerve cells during embryonic life (His; Kohn), the trigeminal ganglions of the skull are derivatives of the gasserian ganglion. As for the ciliary ganglion, Keibel and Mall [3] have demonstrated that its cells are exclusively derived from the gasserian ganglion. The four trigeminal ganglions are, like the gasserian ganglion, homologous to the spinal ganglions. Consequently the long, or sensible, root of the ciliary ganglion is not a real root but a ramus communicans. The sensory root of the ciliary ganglion is really the offshoot of the afferent fibers running from the bulbus oculi toward the brain. The ciliary ganglion is the center for all the sensory impressions coming from the eye, and the only one, since nowhere else in the bulbus can sensory terminations be found (Stoehr). Concerning this concept, based on recent histologic observations, I agree completely with Reichart (1875), Schwalbe (1879), Van Gehuchten (1893) and Pines (1927). The question should, in the meanwhile, be open, whether or not actual sensory ganglion cells, as Pines concluded, are present within the ciliary ganglion. From the standpoint of embryology one must consider the ciliary ganglion a sensory center of the brain shifted to the periphery. This corresponds to the concept of the optic nerve as a dislocated sensory part of the brain, called by some

3. Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, p. 118.

modern authors "fasciculus opticus." The trigeminal ganglions secondarily gain relation to the sympathetic trunk, and so-called sympathetic cells migrate along the oculomotor nerve and the large and small superficial petrosal nerves peripherally. Finally, the small multipolar ganglion cells characteristic of the sympathetic system prevail in these ganglions, giving the impression of real sympathetic ganglions. By my investigations (carried out in collaboration with Pollak [4]) I was taught that the ganglion nodosum vagi, which originally had the character of a spinal ganglion, presents secondarily many "sympathetic cells." This corresponds to the common opinion that in many places outside the gasserian ganglion grouped cells typical of those of the sympathetic nervous system may be found. It is also possible that under certain circumstances ganglion cells remain within the central parts of the brain—the mesencephalic root of the trigeminal nerve is an example. Fibers of the sympathetic trunk may also become displaced centrally and may find connections with the ganglions of the skull. Consequently the sympathetic root of the ciliary ganglion is not a real root. It seems that the so-called sympathetic root of the ciliary ganglion has its synapse within the superior cervical ganglion and passes through the ciliary ganglion without interruption. The following fact seems important to me, although it has nowhere been considered, as far as I know: Whereas all the sympathetic ganglions contain, without exception, chromaffin elements, these elements are missing within the ganglions of the skull. Likewise, the cardiac plexus and its ganglions contain but few chromaffin cells. This fact could prove that one has to deal not with sympathetic but with parasympathetic ganglions, a morphologic proof of the polarity of the vegetative nervous system stressed by Eppinger and Hess. Secondarily the ciliary ganglion gains connection with the oculomotor nerve, which has primarily no relation with sensory cells. Many facts prove that the oculomotor nerve finds a true synapse within the ciliary ganglion. I have pointed out that the number of the small ciliary nerves is larger than that of the entering oculomotor fibers. André-Thomas [5] demonstrated that in cases of tabes dorsalis with far advanced degeneration of the oculomotor nerve the small ciliary nerves were untouched. Severing the oculomotor trunk does not produce degeneration of the small ciliary nerves. Certainly it is possible that, owing to the peculiar structure of the ganglion (similar to that of a syncytium) peripheral degeneration is lacking. The problem is difficult. However, the presence of ganglion cells of the so-called type 2 of Golgi, with small processes going to other cells within the ganglion and the presence of

4. Hess, L., and Pollak, E.: Ztschr. f. d. ges. exper. Med. **48**:724, 1926.

5. André-Thomas, cited by Hovelacque, A.: Anatomie des nerfs craniens et rachidiens et du système grand sympathique chez l'homme, Paris, Gaston Doin, 1927, p. 663.

collateral fibers within the ganglion demonstrates that reflexes of the type of the spinal reflexes may have their anatomic basis within the ciliary ganglion.

The ciliary ganglion is, in my opinion, a primarily sensory organ which finds secondary connections with the parasympathetic system. Its connection with the oculomotor nerve may be a true synapse. Since within the uveal tract and within the ciliary plexus ganglion cells actually cannot be found, I incline to consider the ciliary ganglion and all the neural elements within the bulbus oculi as a unit. *The center for all the nervous impulses arising within the eyeball is the ciliary ganglion.* This would be consistent with the aforementioned law of interruption of the vegetative nerves by *one* synapse. This peculiar neural structure, not comparable to any other organ of the human body, is the basis and the site of the phenomena of acute glaucoma. The bulbus oculi is the terminal organ; the attack is produced outside the eyeball. To explain the events producing glaucoma and to open the way for rational treatment, one must attempt a proof of this concept by analogy, since a more exact demonstration is impossible at present.

PHYSIOLOGIC ANALOGY BETWEEN HARDENING OF THE PENIS IN ERECTION AND HARDENING OF THE GLAUCOMATOUS EYEBALL

The outstanding feature of acute glaucoma is the hardening of the eyeball. The pain (which should not be underestimated) and the effects on the cornea, the pupil and the optic disk are the result of primary hardening and increase of pressure. Hardening is the general sign of all types of glaucoma. For comparison, I like to consider the erect penis as a physiologic model of hardening.

Owing to a psychic excitement within the pathway of a vegetative nerve, the pelvic nerve, acute arterial active hyperemia of the genital organ takes place. The branches of the pudendal artery, carrying the blood to the corpora cavernosa, are characterized by a thick muscle layer and show within their intima special pillow-like strands of longitudinal and sometimes even transverse muscles. By these pillows the lumen of the artery can be blocked or narrowed to a larger extent when the penis is relaxed. With the lumen dilated by the active dilating parasympathetic fibers of the pelvic nerve a large amount of arterial blood can pass freely. Simultaneously with the increased active arterial blood flow the venous return may be retarded by the muscle pillows, which are well developed even in the veins of this area and produce dilatation of the veins. By the simultaneous dilation of the arterial and of the venous vessels the content of blood is enormously increased. In addition, the cavernous spaces, situated in the periphery of the penis, are

mechanically compressed and the venous return is blocked. By contraction of the ischiocavernous muscles blood is driven from the crura penis into the corpora cavernosa, and the pressure within the shaft of the penis is raised. By all these mechanisms the hardening of the penis is achieved. How can the hard organ relax? First, the cavernous spaces in the periphery are opened. A large vein communicating with the central cavernous spaces of the penis is provided wth a recently discovered funnel [6] formed by firm connective tissue. The minute opening of this funnel allows gradual outflow of the blood at the height of the erection and after its relaxation. The orgasm is the effect of the stimulation of the sacral parasympathetic nerves and of their spinal center. The special arteries and veins represent the site of action. By severing of the pelvic nerve or destruction of its center the described mechanism will be abolished, whereas long-standing stimulation results in priapism. With stimulation of the pelvic nerve one may compare, in the case of glaucoma, stimulation either of the parasympathetic or of the sympathetic fibers of the ciliary ganglion. The arrangement of venous sinuses and plexuses in the neighborhood and in connection with the orbit; the numerous capillaries of the ciliary body (which are surprisingly rich in pericytes, providing a large motility under nervous impulses) have been mentioned. It is obvious that the increased content of blood is a contributing factor in the hardening of the eye, in the swelling of the ciliary bodies (with secondary occlusion of the angle of the chamber and its deleterious effect on the circulation of the fluids within the eye) and in the hyperemia of the choroid and the sclera. From the therapeutic standpoint it should be borne in mind that, concerning the double innervation of the eyeball, it is not clear a priori whether the primary stimulation takes place in the sympathetic or in the parasympathetic pathways.

It is of interest that in attacks of acute glaucoma the pressure gradually increases during the night and that the attacks prefer the late hours of night or the early hours of morning. That is the time when, according to general clinical experience, the tendency to the production of visceral paroxysmal crises prevails. Normal labor (a physiologic process), many sexual excitements, the dreadful stenocardia ("stenocardie de décubitus") and cardiac asthma are mostly observed at the same time. In the last-named condition my [7] researches have demonstrated the intervention of parasympathetic nerves. *From these facts I am inclined to believe that a parasympathetic stimulation plays the primary role in glaucoma.* On the other hand, one must remember that many French authors believe that in the sympathetic root of the ciliary

6. Braus, H.: Anatomie des Menschen, ed. 2, Berlin, Julius Springer, 1934, vol. 2, p. 450.

7. Hess, L.: Deutsches Arch. f. klin. Med. **173**:283, 1932; **174**:64, 1933.

ganglion there are vasodilating fibers to the anterior part of the bulbus oculi. By parasympathetic irritation, with its effect of producing alkalosis, a loosening of cell borders and an increased permeability may be enhanced. In accordance with this fact, one finds in epileptic patients an increased fluid content of the brain prior to the attack, which can be demonstrated by encephalogram (Stauder [8]). In the preparoxysmal phase of epilepsy there are definite signs of vagotonia (Eppinger and Hess) whereas during the seizure (a real "sympathetic crisis"), with acidification of the blood, the capillary walls are no longer swollen, and circulation of blood is consequently improved. This hypothesis would correspond with the softening of the eye during the acidotic diabetic coma. The dryness of the brain frequently seen in autopsies of diabetic persons who die in coma and the high content of fluid in the brains of epileptic persons are impressive objective observations.

It is clear that the hardening of the penis, as well as that of the glaucomatous eye, is due to an increased content of fluid within a closed system. Diminished fluid content, outflow of the blood after the erection, dehydration and diminished secretion of the ciliary bodies in the course of severe diabetic coma are associated with relaxation of the penis or of the eyeball, respectively. By opening of the valves during the hardening the pressure and the hardening should be abolished. As to the orgasm, I have mentioned the mechanism of outflow of the blood. The structure of the veins of the bulbus oculi has also been described. By anatomic blockade of the veins of the penis permanent hyperemia and priapism may be produced. In some cases of acute glaucoma, inflammation of Tenon's capsule, with occlusion of venous branches, thrombotic occlusion of the venae vorticosae (Heerfordt), infections of sinuses in the neighborhood of the orbit, periphlebitic processes (Magitot and Bailliart [9]), perforation of the internal carotid artery into the cavernous sinus and sudden increase of the venous pressure have been observed. In accordance with clinical experience, after liberation of the circulation (e. g., in the angles of the chamber) softening of the eye may frequently but not always be achieved. As the underlying cause is situated not there but in the neural pathways, the nervous irritation has to be kept under control. The primary irritation of the parasympathetic pelvic nerve inducing the orgasm is physiologically blocked by the sympathetic antagonist. Likewise, the glaucomatous irritation can be controlled by nerve impulses regulating the circulation of the fluids within the eyeball, except in the presence of anatomic obstruction. In stressing the importance of nervous mechanisms in the problem of

8. Stauder, K. H.: Fortschr. d. Neurol. **8**:1, 1936.

9. Magitot, A., and Bailliart, P.: Ann. d'ocul. **162**:729, 1925; Am. J. Ophth. **8**:761, 1925.

glaucoma two factors are to be remembered. In accordance with a general law of physiology discovered by Exner, after any irritation entering the nervous system the threshold for subsequent irritations is lowered. In this "law of facilitation" the limits of available therapeutic measurements (for surgical treatment is not taken into consideration) are given. The study of glaucoma exclusively from the standpoint of the oculist seems to be too narrow. No biologic phenomenon is isolated; each is a link in an endless chain.

It would take me too far afield should I proceed to demonstrate that in many viscera (liver, spleen, kidney) pathologic conditions comparable to glaucoma are not infrequently encountered. I should like to call attention, however, to the observations of Mauthner and Pick.[10] These authors have found that histamine may produce an occlusion of the hepatic veins at their mouths into the inferior vena cava, with secondary swelling and hardening of the liver. Histamine is a product of protein metabolism and is widely distributed in the body. Besides its action on the hepatic veins, it is a dilator of capillaries and increases their permeability, giving rise to loss of blood plasma and producing edema. The clinical features of occlusion of the hepatic veins previously mentioned—the engorgement and hardening of the liver due to an increased content of blood and an increased extravasation of plasma into the tissue spaces—remind one of the signs of glaucoma. Hence it is of interest that Friedenwald [11] and Rycroft [12] have demonstrated a histamine-like material in the aqueous humor of the glaucomatous patient. These observations, together with hypercholesteremia, slight hyperbilirubinemia and increase of aromatic substances in the blood serum and a positive xanthoprotein reaction of the serum, are indicative of deep metabolic changes associated with an attack of glaucoma. *These metabolic changes may be connected with the disturbances of the vegetative nerves.*

The disorder of the circulation due to histamine or the histamine-like material—the blockade of the hepatic veins—is relieved by the sympathotropic epinephrine. It is known that by histamine an increased outflow of epinephrine from the adrenal glands is reflexly produced. This is of interest because of the use of epinephrine as recommended by Hamburger in the treatment of glaucoma. It is possible that in some particular cases of glaucoma—not in all—primary irritation of parasympathetic nerve fibers needs a curative counteraction by the sympathetic antagonist.

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10. Mauthner, H., and Pick, E. P.: München. med. Wchnschr. **42**:1141, 1915. Arey, L. B., and Simonds, J. P.: Anat. Rec. **18**:219, 1920.

11. Friedenwald, J. S.: Pathogenesis of Acute Glaucoma, Arch. Ophth. **3**:560 (May) 1930.

12. Rycroft, B. W.: Brit. J. Ophth. **18**:149, 1934.

Moreover, in recent years it has been proved that nerve fibers coming from the carotid sinus influence the general blood pressure. The carotid sinus nerves have close connection with the superior cervical sympathetic ganglion. This ganglion is the origin of the sympathetic "root" of the ciliary ganglion. An influence on the vessels of the eye and on their motility by the carotid sinus should also be taken into consideration.

I have suggested that in an attack of acute glaucoma following a primary stimulation of parasympathetic nerve fibers a sympathetic counteraction sometimes takes place. In epileptic seizures this mighty change from parasympathetic to sympathetic stimulation is impressive. This is particularly obvious in those cases of epilepsy in which the seizures are almost exclusively observed at the time of digestion, when assimilatory processes, with increased activity of the parasympathetic vagus nerve, necessarily produce a counteraction of sympathetic fibers.

CONCLUSIONS

1. Acute glaucoma is a neurovascular condition dominated by the ciliary ganglion.

2. Glaucoma has its analogy in certain pathologic changes of the liver, the kidney and the spleen.

3. In the clinical picture of acute glaucoma one must differentiate primary irritation and secondary spontaneous counteraction.

4. The ciliary ganglion and the ciliary plexus are to be considered as a unit.

ORTHOPTICS

CLINICAL EVALUATION OF RECENT ADVANCES

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The term "orthoptics" has been used by various authors to cover every phase of the treatment of strabismus, even the operation. I prefer to reserve the use of it for the nonsurgical treatment, but, believing that there is general agreement as to the employment of glasses and occlusion, I intend to confine my remarks to the portion of the work usually allotted to the orthoptic technician.

The ophthalmologist's problem is to try to evaluate orthoptics. A fair appraisal of orthoptic methods is a task that has confronted ophthalmologists for many years, and it remains a challenge to those who have taken special interest in this work.

Written reports of results of orthoptic treatment are provocative but far from convincing in the majority of instances. The great variation in the classification of cases; the lack of concise definitions of terms and methods, and the complete absence of unanimity as to criteria for cure are among the factors that make confusion inevitable. Yet it is impractical for one physician to visit several clinics for sufficient periods to enable him to judge results by personal observation; so one is forced to rely largely on the literature for the data. The symposium on orthoptic training held at the Oxford Congress in 1939 and published in the second volume of the transactions of the Ophthalmological Society of the United Kingdom for that year is one of the best recent contributions to the subject, as it includes discussions by many of the leading exponents as well as by some of the most articulate critics of this subject in England. However, it illustrates the difficulty of the problem of evaluation, for, after a fairly heated discussion, it was quite evident that not one of the physicians participating had changed his opinion in the least, and the reader is left with several questions and some doubts but no convictions that he did not have originally.

Space is lacking for a full discussion of the arguments for and against orthoptics. I can give only my conclusions, reached from a careful survey of the literature and from discussions with many oculists and orthoptic technicians both in the United States and in Great Britain.

Read before the Section of Ophthalmology, New York Academy of Medicine, Jan. 20, 1941.

In the United States much less is being written on orthoptics today than six to eight years ago when the names of Guibor, Bressler and others became familiar. Recent articles have dealt more with the technical aspects of the subject than with the results obtained. A possible explanation of this is that the earlier reports, which were perhaps a little premature, have not been supported by subsequent investigation. While there is still a great deal to be learned, much has been accomplished by the various clinics throughout the country toward establishing the indications for, and the limitations of, orthoptic training. Accord- to Hardy, among the well established, generally accepted uses of orthoptics are:

1. Development of procedures for the diagnosis, prevention and cure of anomalous retinal correspondence.

2. Development of simultaneous macular perception.

3 Development of fusion and fusion amplitude.

4. Stabilization of the binocular coordinations in the primary and secondary positions of gaze.

Of recent developments, the following five are particularly important:

1. Orthoptic councils, made up of ophthalmologists, who investigate orthoptic procedures and regulate the training of technicians, have been founded both in the United States and in Great Britain. These councils are doing much to put this form of therapy on a firm foundation and to establish the proper relation between ophthalmologists and technicians.

2. The publication of the first orthoptic journal, by the English in 1939, with articles by both ophthalmologists and technicians, has helped to standardize physicians' ideas.

3. The proposed standard of cures [1] submitted by the British orthoptists to their council should be valuable in clarifying the problem.

4. The symposium for physicians and technicians at the meeting of the American Academy of Ophthalmology in the fall of 1940 was an important milestone.

5. The recent appearance of the second edition of Lyle and Jackson's book "Practical Orthoptics" [2] is particularly fortunate, as this is undoubtedly the best textbook for the beginner in this work.

Few ophthalmologists will take issue with the theoretic basis of orthoptics. It must be admitted that in isolated instances almost every type of squint has been cured or materially benefited by orthoptic training. But the practical limitations of the system are an entirely different

1. Standard of Cures, Brit. Orthop. J. **1**:113, 1939.

2. Lyle, K., and Jackson, S.: Practical Orthoptics in the Treatment of Squint, London, H. K. Lewis & Co., Ltd., 1940.

question, and this is the question that interests most ophthalmologists. Should the ophthalmologist use orthoptics in his daily practice, and if so, how? The importance of binocular single vision in everyday life is beyond the scope of this paper, but most persons will agree that physiologic cure of strabismus is desirable if it is practically possible.

It is my definite impression that the majority of orthoptic workers today believe that, with the exception of accommodative squint, it is rarely practical to try to cure a tropia by orthoptic training alone. The majority favor a short, intensive course of training to try to correct abnormal retinal correspondence, remove suppression and develop fusion with amplitude. The preliminary training may be continued as long as there is improvement. If no improvement is obtained or if improvement is arrested, operation is done, to be followed a week later by exercises taken daily for about two weeks and then less frequently for a period to be determined by the conditions in the individual case. This is an ideal program, to which no theoretic objections are raised. Undoubtedly, if binocular single vision with fusion and some amplitude can be acquired either before or after operation, it will not only give a more perfect result but contribute greatly toward permanence.

Some of the practical obstacles to this program should be considered. It is generally conceded that exercises should not be undertaken without certain fundamental pieces of equipment or without the supervision of one specially trained for this work. This is chiefly because of the great danger that abnormal retinal correspondence will be undiagnosed or improperly handled. The essential equipment is expensive and requires additional floor space, which is frequently costly. Few ophthalmologists have the time or the temperament to carry out routine exercises; so a trained technician becomes a necessity. Not many ophthalmologists have a sufficient number of cases of squint to justify these additional expenses. The ideal solution would seem to be the pooling of resources by a group of oculists and the installation of a technician in a separate office, where patients may be referred for training. This has been done with notable success in San Francisco and in several other cities. However, at present this makes orthoptics available to only a small percentage of ophthalmologists. Add to this the expense to the patient, the time which he (and usually a parent) must spend in coming for exercises, the possibility of failure and the occasional harmful result from prolonged training, and the weight on the debit side becomes imposing.

It is with accommodative squint that orthoptists report uniformly favorable results. Recent publications by Davis have emphasized the satisfactory results obtained by teaching the patient to dissociate the accommodation and convergence. Yet it is for this same condition that glasses and occlusion have been most helpful; hence the importance of

the exercises has been questioned, and the problem of evaluation is still extremely difficult. In this connection I should like to raise an objection that also applies to the teachings of Lyle and several of his English confreres, namely, that exercises are rarely worth while for children under the age of 7 years. To my mind, the treatment of strabismus should be carried out at the earliest possible moment, and to mark time, even with precautionary measures, is to risk serious damage, both psychic and physical.

From a purely diagnostic and prognostic point of view, orthoptic methods and the major amblyoscopes have opened new possibilities. Abnormal retinal correspondence has become a familiar term; yet its profound influence on operative results is just beginning to be realized, to mention only one of its potentialities. More complete diagnoses of the state of binocular function are possible, providing for more exact etiologic classifications and giving information that should aid greatly in the operative handling of the abnormalities involved. Full utilization of this information must await more investigation.

The orthoptic treatment of phorias is even more difficult to evaluate. While the reports are almost unanimously favorable, there is little agreement as to the indications, and convergence insufficiency is the one type of phoria that all agree is definitely benefited by exercises. Results are measured largely by the relief of subjective symptoms; so that any sort of analysis becomes practically impossible.

CONCLUSIONS

I should like to emphasize the following points:

Orthoptic methods give valuable information about binocular function, which with further experience should prove a guide in the operative treatment.

Orthoptic training is on a much firmer footing than it was a few years ago, but its indications and limitations need further defining.

Orthoptic training should be carried out only by a qualified technician with the proper equipment under the supervision of an ophthalmologist.

Practical considerations greatly limit the application of orthoptic methods; at present, therefore, it is impractical for the average practitioner to use them routinely.

Research clinics should be encouraged to continue in as many institutions as possible, for by the building up of a large mass of data the answers to the questions presented may be reached.

DISCUSSION

DR. JAMES W. WHITE: I agree with practically everything which Dr. Wheeler has said, but he failed to distinguish between ocular and systemic types of convergence insufficiency. In cases of the systemic

type orthoptic training does little or no good and often makes the patient more uncomfortable until the cause of the condition is removed.

DR. LEGRAND H. HARDY: The greatest single factor in the failures of orthoptics has been misapplication of method, or ignorance of what can and may be expected.

The element of personality, by which one technician or oculist may achieve by the same methods results differing greatly from those obtained by another technician or oculist who is less enthusiastic and less inspiring, makes the evaluation very difficult. Orthoptics is a learning process and is conditioned by all or many of the impediments which accompany any other learning process.

Ophthalmologists beginning orthoptic treatment should select patients with heterophorias, with which the danger of misapplication is least. To permit a patient with anomalous retinal correspondence to carry out any binocular training procedures which are not carefully supervised by an alert and well trained technician is simply to invite failure and can serve only to confirm the squint rather than to cure it. Such misapplication and its results have stigmatized the whole subject in the opinion of many honest surgeons.

Orthoptic training has a definite place in ophthalmology, and I hope that through the efforts of the American Orthoptic Council it will be reclaimed for this specialty.

SUITING THE CYLINDER TO THE MIRROR IN RETINOSCOPY

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Retinoscopy can be practiced with either a plane or a concave mirror. Of the latter there are two types, the usual short focus concave and the occasionally used long focus concave. With the latter the light directed to the patient's eye is convergent, but to a relatively slight extent. It must be used so that the light tends to focus behind the patient. Unless one is very careful the incident convergent light, instead of focusing behind the patient, may tend to focus in the plane of the patient's eye (strictly speaking, in the plane of the pupil). This leads to a confusing phenomenon, for in this case no motion is observed whatever the condition of the patient's eye. It gives rise to what may be called the "incident neutral point." For there is a neutral point for the incident light, just as there is one for the emergent light. This phenomenon, first described by Marquez explains the sometimes puzzling absence of light and shadow movements in ametropic eyes when a concave mirror is used. This is one reason why the long focus concave mirror, although best in some special instances, has practically gone out of use.

The short focus concave mirror produces a real image of the retinoscopic light source, situated between the examiner and the patient. This real, aerial image of the light source becomes the immediate source of the light thrown into the patient's eye. If one designates by L′ the image of the real light source in retinoscopic examination, then when a plane mirror is used L′ is behind the examiner. When a concave mirror is used L′ is in front of the examiner. In both cases L′ is the immediate source of light for illuminating the patient's retina. To determine the bearing which this fact has on astigmatic corrections and the choice of a cylinder for neutralization, the following considerations may be mentioned:

An accepted principle of retinoscopy is that for the easiest determination of astigmatism there must be a certain relation between the "vergency" of the light incident on the patient's eye and the "vergency" of the light which emerges from the patient's eye. The emergent light in an astigmatic eye tends to form two focal lines at different distances, one focal line at the far point (the retinoscopically neutral point) of

each of the two principal meridians. To obtain neutralization the two far points must be made real, that is myopic, if necessary, by over-correction (with plus lenses) of inherent hyperopia. Therefore, one may speak of the two principal meridans as being myopic to different degrees. The far point of the less myopic meridian is farther from the patient's eye than is the far point of the more myopic meridian.

When one meridian of the patient's eye is in focus for the incident light from L′ (whether L′ is in front of or behind the examiner) and the examiner's eye is in focus for the light emerging from the other meridian of the patient's eye, the banded, straight-edged appearance of the reflex light and shadow is most marked. This is the relation of the "vergency" of the incident light to the "vergency" of the emergent light which is best for astigmatic observation. For example, if the patient has 2 D. of myopia in the vertical meridian and 1 D. of myopia in the horizontal meridian, the characteristic astigmatic phenomena are most marked either when L′ is at 1 meter and the examiner is at 50 cm. from the patient or when L′ is at 50 cm. and the examiner is 1 meter from the patient. In either of these arrangements one meridian of the patient's eye is in focus for L′ and the examiner's eye is in focus for the other meridian. It is evident that this relation can be obtained with either a plane or a concave mirror but that the cylinder to be used for neutralization must be different for the two mirrors. For instance, in the aforementioned example, if a plane mirror is used, the examiner must first neutralize the more myopic meridian (the vertical meridian) at 50 cm.; the less myopic (horizontal) meridian will then be in focus for L′ 1 meter from the patient. The examiner must now use a plus cylinder (+1.00 D. cyl., axis 90) to neutralize the "with" movement in the less myopic (horizontal) meridian. If a concave mirror is used, the examiner must first neutralize the less myopic meridian (the horizontal meridian) at 1 meter. The more myopic (vertical) meridian will be in focus for 50 cm. from the patient. The examiner must then use a minus cylinder (—1.00 D. cyl., axis 180) to neutralize the "with" movement in the more myopic (vertical) meridian.

In the foregoing example it was assumed that L′ behind the plane mirror is 1 meter from the patient's eye and that L′ in the concave mirror is 50 cm. from the patient's eye. These positions must be especially arranged. But the fundamental point which applies in all cases is that with a plane mirror to bring out the astigmatic phenomena it is best to neutralize first the more myopic meridian with a sphere and

then use plus cylinders to neutralize the less myopic meridian. By this arrangement the focus for the less myopic meridian, being behind the examiner, will be near L′ or may even coincide with it. With a concave mirror (short focus) it is best to neutralize first the less myopic meridian with a sphere and then use minus cylinders to neutralize the more myopic meridian. By this arrangement the focus for the more myopic meridian, being in front of the examiner, will be near L′ or may even coincide with it. This method of correlating the kind of cylinder used with the kind of mirror used is especially useful since the new luminous retinoscopes enable the retinoscopist to use a plane or a concave mirror at will.

GONORRHEAL OPHTHALMIA

TREATMENT WITH A SULFANILAMIDE DERIVATIVE* AND INJECTIONS OF MILK

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AND
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Before the advent of sulfanilamide and its derivatives into the field of ocular therapy, patients with gonorrheal ophthalmia in St. Luke's Hospital No. 2 were treated by copious and frequent irrigations of the conjunctival sacs, local applications of antiseptics and injection of non-specific foreign proteins. Of the last-mentioned substances, milk was subjected to the most thorough trial. With its use in the treatment of gonorrheal ophthalmia, formerly cured in from one to two months with local therapy alone, only about two weeks is now required for the eyes to become clinically cured and for conjunctival smears to fail to show gonococci.

A year ago, prompted by the encouraging reports [1] appearing in medical literature on the use of sulfanilamide and sulfanilyldimethyl-sulfanilamide in the treatment of gonorrheal ophthalmia, we began giving sulfanilamide, in addition to the usual local treatment and foreign protein therapy, to our hospitalized patients with gonorrheal ophthalmia. The rate at which recovery took place and the gonococci disappeared from the conjunctiva was so rapid that we began treating patients in a similar manner in the outpatient department. We found that patients

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From the Ophthalmology Department of St. Luke's Hospital No. 2.

Read at the combined clinical conferences of St. Luke's hospitals No. 1 and No. 2 and of St. Elizabeth hospitals on Dec. 19, 1940.

* The compound used was sulfanilyldimethylsulfanilamide. This is the most widely used drug in Germany for the treatment of gonorrhea. There is as yet no definite clinical evidence that it possesses any advantage over sulfanilamide or sulfapyridine in the treatment of this disease.

1. Walker, C. J.: Am. J. Ophth. **21**:1041, 1938. Fernandez, L. J., and Fernandez, R. F.: ibid. **21**:763, 1938. Michels, M. W.: J. Pediat. **13**:527, 1938 McKee, S. H.: Gonorrheal Ophthalmia Cured After One Week's Treatment with Sulfanilamide, Arch. Ophth. **21**:1035 (June) 1939. Bowers, A. G., and Frank, W.: Am. J. Ophth. **22**:277, 1939. Prettin, H.: Klin. Monatsbl. f. Augenh. **102**: 114, 1939; abstracted, Am. J. Ophth. **22**:700, 1939. Rein, W. J., and Tibbetts, O. B.: ibid. **22**:1126, 1939.

without corneal lesions usually became symptom free after about six days of treatment and without corneal complications ever occurring during the time of observation. We made no attempt to study them systematically until recently, when we were afforded the opportunity to observe the results of injections of milk and oral doses of sulfanilyldimethylsulfanilamide in 17 cases of gonorrheal ophthalmia during an epidemic in a nearby children's receiving home. The infrequency of reports of epidemics of gonorrheal ophthalmia in recent years, due to improved hygienic conditions, together with the comparatively new use of chemotherapy in the treatment of such conditions and an ideal opportunity for a comparative and controlled study, all prompted us to report our observations in this small series of cases.

CLINICAL MATERIAL

Seventeen patients ranging from 4 to 9 years in age, each weighing from 22 to 41 pounds (10 to 19 Kg.), with red, swollen and discharging eyes of about ten days' duration, were sent to our ophthalmic outpatient department for treatment. Examination of conjunctival smears showed the presence of gonococci in all of them.[2] They were hospitalized and put into a single ward especially arranged for their exclusive use. The usual isolation precautions were maintained for each patient. Further examination of these children revealed no extraocular gonorrheal infection. All of them were underweight and undernourished.

The duration of the disease before admission ranged from seven to twelve days. All of the children but 1 were infected binocularly. When first seen, most of them had marked purulent discharge with blepharospasm and edema of the lid. In 15 of them both corneas were intact. Three had monocular corneal involvement; one, a shallow ulcer; another, anterior synechia and fistula, and another, ulceration and partial anterior corneal staphyloma.

PROCEDURE

Our study was an attempt to learn the relative value of (1) injections of milk, as employed by us formerly, (2) chemotherapy (sulfanilamide and its derivatives), found by so many authors to give favorable results, and (3) a combination of the two methods, which we have in the recent past months employed so successfully for our hospitalized and dispensary patients. We divided the patients into three groups according to the type of treatment given. The patients were grouped according to their age, regardless of the severity of their ocular infection. All of them were given irrigations of potassium permanganate in a dilution of 1 : 5,000 as frequently as was necessary to keep the conjunctival sacs clean. No other local medications were given except atropine drops in cases in which there was corneal involvement. Five patients (group 1), aged 4 to 5 years, were given intragluteal injections of 4 to 7 cc. of boiled milk on the first, second, fourth and fifth day. Five patients (group 2), aged 8 to 9 years, were

2. Subsequent investigations by members of our social service department revealed that the source of infection was most probably a child with gonorrheal vaginitis of two months' duration in the children's receiving home, who was also hospitalized for treatment.

given 2 Gm. of sulfanilyldimethylsulfanilamide by mouth every twenty-four hours for five days. Seven patients (group 3), aged 6 to 7 years, were given intragluteal injections of 8 to 9 cc. of milk on the first, second, fourth and fifth day together with 2 Gm. of sulfanilyldimethylsulfanilamide orally every twenty-four hours for a total of 8.5 Gm.

We found it necessary at the end of a week's observation to institute the combined treatment of milk injections and sulfanilyldimethylsulfanilamide orally in all of the patients in group 1 and in 2 of those in group 2, in order to shorten the period of study. The necessary examinations of blood and urine were made every other day in patients given the sulfanilamide derivative. Conjunctival smears were obtained every day for microscopic examination for gonococcus, and three consecutive negative smears were taken as the chief criterion for the cure of the disease.

RESULTS

Group 1 (patients given injections of milk): The 5 patients in this group all had intact corneas, and no complications developed during the course of treatment. The temperature at its height varied from 100 to 104 F. No noticeable ill effects were observed in the patients beyond that of slight redness and some tenderness at the site of injection. Marked improvement in swelling of the lids, blepharospasm and discharge occurred twenty-four hours after the first injection. It was most noticeable after a forty-eight hour period, after which the rate of improvement became very slow, despite the fact that good fever reactions of around 102 F. could still be obtained by increasing the amount of milk injected by 1 or 2 cc. At the end of a week's observation, we found that the patients could open their eyes fairly well; edema of the lids was practically gone, and the discharge was much decreased, but still evident. Gonococcus could still be detected in the conjunctival smears, but in much smaller numbers. Sulfanilyldimethylsulfanilamide, 1.5 Gm. daily, was then administered orally, and another injection of milk was given.[3] In all patients the discharge cleared up in from twenty-four to forty-eight hours. The first of three consecutive negative smears was obtained in twenty-four hours from 3 patients and in seventy-two hours from 2 after the first day of administration of the drug. A total of 8 Gm. of the sulfanilamide derivative was given to these patients before they were discharged. No relapses occurred.

Group 2 (patients given sulfanilyldimethylsulfanilamide): Two of the 5 patients in this group had corneal complications; one had a perforated corneal ulcer with partial anterior corneal staphyloma in the left eye, while the second had a shallow ulcer in the left eye. Drops of 1 per cent atropine sulfate solution were instilled in the eyes of these patients. Of the 3 patients with uncomplicated corneas, 2 became entirely free from discharge on the third day and the other on the fifth

3. This was probably unnecessary.

day. The first of three consecutive negative smears was obtained on the fourth day from 1 patient and on the fifth day from the other 2. In regard to the 2 patients with corneal complications, a corneal ulcer developed in the periphery of the cornea in the uncomplicated right eye of 1 of them on the fourth day of therapy, proceeding rapidly on to a small perforation with prolapse of the iris, which was reduced after energetic atropinization and trichloroacetic acid cautery. The shallow ulcer on the left cornea of this patient, however, healed on the sixth day of therapy. The corneal condition of the second patient showed no marked improvement. After one week's observation, in both patients, although there was general improvement, the eyes were still discharging, there was some blepharospasm, and the smears showed gonococci. The combined treatment, with administration of sulfanilyldimethylsulfanilamide by mouth plus injections of 7 to 9 cc. of milk in the usual time interval, was then given them. Four days after the combined treatment was begun the eyes of these patients were entirely free from discharge, and the first of three negative smears was obtained on the fifth and sixth day of treatment respectively. The corneal complications responded rapidly to this second course of treatment but required, in addition, the use of trichloroacetic acid cautery to flatten the prolapse and the partial anterior corneal staphyloma.

The only toxic manifestation ever observed in our three groups of patients from the use of the sulfanilamide derivative occurred in these 2 patients when, during the second course of treatment after ingestion of 5.5 Gm. of the drug in addition to the 10 Gm. already taken in the first course of treatment, mild abdominal pain with loss of appetite and malaise were complained of. Immediate stopping of the use of the drug and forcing of fluids cleared up the condition within ten hours. No peripheral neuritis or other signs of toxic manifestation were ever observed by us. No abnormal changes in the urine or blood were ever reported.

Group 3 (patients given combined treatment): Of the 7 patients in this group, only 1 had a corneal complication, consisting of a small perforated ulcer in the left eye with anterior synechia and fistula. The condition cleared up two days after the beginning of treatment, with the additional use of atropine eye drops, which broke the anterior synechia. With the combined form of treatment, a clinical cure, with disappearance of the discharge, the edema of the lids and the blepharospasm, was obtained in three days in 4 patients,[4] in four days in 2 patients and in

4. The right eye, with an intact cornea, of 1 of the patients with corneal complication became clinically cured on the third day of treatment, while the left eye, with the corneal ulcer, required six days.

Results of Treatment with Injections of Milk and Administration of Sulfanilyldimethylsulfanilamide in Cases of Gonorrheal Ophthalmia

Case	Corneal Involvement Before Treatment	First Course of Treatment				Second Course of Treatment (Sulfanilyldimethylsulfanilamide Orally and Milk Intragluteally)	
		Medication	Disappearance of Discharge	Negative Smear *	Corneal Complications	Disappearance of Discharge	Negative Smear *
1.....	None	Milk injections	Still present at end of seven days	Still positive at end of seven days	None	First day †	First day
2.....	None	Milk injections	Still present at end of seven days	Still positive at end of seven days	None	Second day	First day
3.....	None	Milk injections	Still present at end of seven days	Still positive at end of seven days	None	Second day	First day
4.....	None	Milk injections	Still present at end of seven days	Still positive at end of seven days	None	Second day	Third day
5.....	None	Milk injections	Still present at end of seven days	Still positive at end of seven days	None	Second day	Third day
6.....	Ulcer with anterior staphyloma	Sulfanilyldimethylsulfanilamide orally, 2 Gm. in 24 hr. for a total of 10 Gm.	Still present at end of seven days	Still positive at end of seven days	None	Fourth day	Fifth day
7.....	None		Third day	Fourth day	None	.....	.....
8.....	Shallow ulcer of the left eye		Still present at end of seven days	Still positive at end of seven days	Perforated ulcer with prolapsed iris (right eye)	Fourth day	Sixth day
9.....	None		Fifth day	Fifth day	None	.....	.....
10.....	None		Third day	Fifth day	None	.....	.....
11.....	None	Milk injections combined with sulfanilyldimethylsulfanilamide orally (2 Gm. in 24 hr. for a total of 8.5 Gm.)	Fifth day	Fifth day	None		
12.....	None		Fourth day	Fifth day			
13.....	None		Fourth day	Sixth day			
14.....	None		Third day	Fifth day			
15.....	None		Third day	Fifth day			
16.....	None		Third day	Fifth day			
17.....	Perforated ulcer with fistula of the left eye		Third day (right eye) Sixth day (left eye)	Fifth day (right eye) Tenth day (left eye)			

* First day of three consecutive days with negative smear for gonococci.
† First day after institution of combined treatment and the eighth day after initial treatment of ocular infection.

five days in 1 patient. Five patients had the first of three consecutive negative smears on the fifth day and 1 on the sixth day, and in the other patient conjunctival smears from the eye with the corneal complication—although the eye had appeared healed clinically after six days of treatment—continued to show one or two gonococci until the tenth day. No further treatment was given to this group of patients, and no relapses were observed.

COMMENT

Our observations on this small series of patients have shown the results of oral administration of sulfanilyldimethylsulfanilamide combined with injections of milk as compared with those of administration of the drug alone to be about the same in patients with gonorrheal ophthalmia uncomplicated by any corneal lesions. But the use of the drug alone in 1 patient did not prevent the formation of a corneal ulcer, which proceeded until it caused perforation and prolapse of the iris during the course of treatment. It is significant that no corneal complications occurred in group 1, in which injections of milk were used alone, although the discharge from the eyes, however markedly decreased after this therapy, continued to be present after seven days of treatment, with persistence of gonococci in the conjunctival smears. No corneal complications occurred in group 3 in which injections of milk in addition to administration of the sulfanilamide derivative was employed. This method appears to be more effective than giving the drug alone in treatment of corneal complications, as shown by the rapid healing of 2 patients in group 2 with corneal complications and of 1 patient in group 3 with corneal perforation and fistula. In group 1 the first two injections of milk appeared to be most effective, while the last two injections did not improve the condition to any significant extent. It appears to us that when it is used in combination with chemotherapy, two injections may be all that is necessary.

The use of milk in the treatment of ocular conditions was first introduced, by Schmidt, in 1915.[5] Since then many favorable reports [6] have appeared in medical literature from all over the world. Our results with injections of milk alone show that purulent discharge diminishes very rapidly after the first and second injections, as stated by Pillat [6b] and Luo,[6d] but, contrary to their observation that negative smears could be obtained from three to five days after the injections were begun, all our

5. Schmidt, R.: Med. Klin. **12**:171, 1916.

6. (*a*) Müller, L.: Wien. klin. Wchnschr. **31**:933, 1918. (*b*) Pillat, A.: Klin. Monatsbl. f. Augenh. **70**:289, 1923. (*c*) Hradecka, J., and Knobloch, R.: Československ. oftal. **2**:190, 1935; abstracted, Am. J. Ophth. **20**:84, 1937. (*d*) Luo, T. H.: Chinese M. J. **50**:27, 1936.

* First day of three consecutive days with negative smear for gonococci.
† First day after institution of combined treatment and the eighth day after initial treatment of ocular infection.

patients continued to have a few gonococci on the smears after seven days of treatment. Von Hippel [7] stated that injections of milk are best for the effect on diminution of purulent discharge, although this treatment does not cause the uncommonly fast disappearance of the gonococcus. The action of nonspecific foreign protein therapy is at present unknown, although many theoretic explanations have been offered. It may be that the gonococcus is either killed or attenuated in its virulence, owing to a variety of enzymes or antibodies produced through the stimulation of the general defence mechanism by the cleavage products of the milk and mobilized especially toward the focus of infection, where the capillaries on account of the disease already have an increased permeability. The histologic research of von Szily [8] showed that an injection of nonspecific foreign protein causes widespread inflammatory changes in the structure of the eye characterized by a vasodilation, a lymphocytosis and a diffuse cellular infiltration. The evidence points toward a strengthening and augmentation of the local defense mechanism through the use of foreign protein therapy.

The use of sulfanilamide and its derivatives is definitely of benefit in cases of gonorrheal ophthalmia, as shown by the many favorable reports in medical literature and in our own limited experience. The manner in which these drugs act is still under investigation. According to Long and Bliss,[9] it seems possible to conclude that sulfanilamide and its derivatives do not arouse a specific response on the part of the host. The production of antibodies is not stimulated, and there is no direct action on the phagocytic mechanism. On the other hand, there is considerable evidence that the drug acts on the micro-organisms in vitro and in vivo. Some investigators are of the opinion that this action takes the form of an inhibition of the growth of the bacteria, which brings about a suppression of their invasive power and thereby permits the defense mechanism of the host to accomplish its function.

Therefore, the more rapid healing of corneal complications and the absence of recurrences during the course of treatment with injections of milk in combination with oral doses of sulfanilyldimethylsulfanilamide, as observed in our series of cases, may possibly be explained by the complementary action of these two forms of therapy. It appears rational, therefore, that in treatment of gonorrheal ophthalmia, a combination of two forms of therapy is desirable, especially in cases of corneal com-

7. von Hippel, in Axenfeld, T.: Lehrbuch und Atlas der Augenheilkunde, edited by E. Hertel, ed. 8, Jena, Gustav Fischer, 1935, p. 276.

8. von Szily, A.: Klin. Monatsbl. f. Augenh. **85**:21, 1930.

9. Long, P. H., and Bliss, E. A.: The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds, New York, The Macmillan Company, 1939, p. 132.

plication, whereby one inactivates the invading organism while the other stimulates the body defense mechanism to bring the condition under a quicker, uneventful and more successful control.

SUMMARY AND CONCLUSIONS

Seventeen children with epidemic gonorrheal ophthalmia from a children's receiving home were hospitalized and divided into three groups for study.

Five patients (group 1) were given four injections of milk intragluteally. The ocular infection improved markedly under this treatment but still persisted after one week's observation. Sulfanilyldimethylsulfanilamide orally was then given with another injection of milk to shorten the period of study. After one to two days of this treatment all the patients were cured. No complications occurred.

Five patients (group 2) were given sulfanilyldimethylsulfanilamide orally, and 3 of them had the first of three consecutive negative smears for gonococcus in four to five days. Two children with corneal involvement before treatment continued to show discharge and positive smears for gonococcus during treatment with the drug alone. They required a second course of treatment, consisting of injections of milk together with oral administration of the sulfanilamide derivative to cure the infection after five and six days respectively of the latter treatment. In 1 of these 2 a corneal ulcer developed which perforated during treatment with the drug alone.

Seven children (group 3) were given a combination treatment with sulfanilyldimethylsulfanilamide orally and milk intragluteally. Five of them had the first of three consecutive negative smears for gonococcus on the fifth day, 1 on the sixth day and the last, with corneal involvement, on the tenth day, although the eye was clinically cured on the sixth day. No complications occurred during treatment.

It is shown that a combination treatment consisting of oral administration of sulfanilyldimethylsulfanilamide and injections of milk is superior to injections of milk alone in the more rapid rate of cure and to administration of the drug alone in the prevention and healing of corneal complications. Under such combined therapy, five to seven days of chemotherapy with two injections of milk are probably sufficient to cure uncomplicated gonorrheal ophthalmia in the acute and subacute stages without danger of relapse. Patients with corneal complications will require four injections of milk and possibly up to ten or twelve days of chemotherapy.

EFFECT OF OXYGEN DEPRIVATION AND STRYCHNINE ADMINISTRATION ON VISUAL FUNCTION

A STUDY OF THE ANGIOSCOTOMAS

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Numerous investigations of the effect of a reduction in atmospheric pressure or in the percentage of oxygen have been made on human beings. Studies made both in mountain expeditions and at sea level have shown not only that the entire organism is affected under such conditions but, more specifically, that the greatest effect appears to be on the central nervous system.[1] The great interest in visual function under these conditions shown in the literature stems not alone from its practical significance in aviation but from the fact that the eye morphologically and metabolically is an extension of the brain.

During the first World War numerous studies were undertaken to determine the effect of oxygen deprivation on visual function. The results indicated some impairment at relatively high altitudes. The methods, however, were crude and not always well controlled. More recently, Goldmann and Schubert[2] found a considerable increase in the difference thresholds for brightness of a test object. McFarland and Edwards,[3] employing the Reeves smoked glass wedge, objectively

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* Fellow in Ophthalmology, Long Island College of Medicine.

The Linde Air Products Company supplied oxygen and nitrogen.

Read at a meeting of the American Psychological Association, State College, Pa., Sept. 5, 1940.

This research was carried out in the Psychophysiologic Laboratories of the Department of Psychology, Columbia University.

From the Department of Psychology, the University of Alabama (Dr. Seitz) and the Department of Ophthalmology, the Long Island College of Medicine (Dr. Rosenthal).

1. Heymans, C., and Bouckaert, J. J.: Sur la survie et la réanimation des centres nerveux, Compt. rend. Soc. de biol. **119**:324-326, 1935.

2. Goldmann, H., and Schubert, G.: Untersuchungen über das Gesichtsfeld bei herabgesetztem Sauerstoffdruck der Atmungsluft, Arch. f. Augenh. **107**:216-237, 1933.

3. McFarland, R. A., and Edwards, H. T.: The Effects of Prolonged Exposures to Altitudes of Eight to Twelve Thousand Feet During Trans-Pacific Flights, J Aviation Med. **8**:3-24, 1937.

demonstrated impairment in light sensitivity, and Gellhorn,[4] using Masson disks,[5] found changes in brightness sensitivity in the presence of acute anoxia.

With refinement in technics it became increasingly evident that visual function deteriorates at high altitudes or under artificially created conditions simulating high altitudes. The problems became more elaborate, and interest was shown in the nature and locus of the change. Fischer and Jongbloed[6] studied dark adaptation to determine, among other things, whether the disturbances noted under oxygen deprivation are due to alterations in the nervous system or to some other tissue change. They concluded that oxygen deprivation modifies the photochemical substances of the retina. The rapid return to normal threshold values following the administration of oxygen was interpreted as evidence for the resynthesis of this substance.

Bunge,[7] studying dark adaptation under somewhat different conditions, stated, with more logical and experimental justification, that the effect of oxygen deprivation on visual function is other than photochemical. McFarland and Evans,[8] in a well controlled experiment involving a more impressive number of subjects, substantiated the claims of Bunge.

Evans and McFarland,[9] using the technic of angioscotometry, noted progressive changes in the perimacular field with increasing depletion of the available oxygen supply. The alterations were attributed to retinal synaptic dysfunction rather than to edema or to changes in the size of the capillaries.

As part of a more elaborate study of flicker fusion under conditions of anoxemia, one of us (Seitz[10]) showed that the effect of the direct

4. Gellhorn, E.: The Effect of O_2-Lack, Variations in the Co_2-Content of the Inspired Air and Hyperpnea on Visual Intensity Discrimination, Am. J. Physiol. **115**:679-694, 1936.

5. The Masson disk consists of a white circle along one radius of which black squares are spaced. When it is rotated, a series of concentric rings of diminishing degrees of grayness appear.

6. Fischer, F. P., and Jongbloed, J.: Untersuchungen über die Dunkeladaptation bei herabgesetztem Sauerstoffdruck der Atmungsluft, Arch. f. Augenh. **109**: 189-196, 1935.

7. Bunge, E.: Verlauf der Dunkeladaptation bei Sauerstoffmangel, Arch. f. Augenh. **110**:189-196, 1936.

8. McFarland, R. A., and Evans, J. N.: Alterations in Dark Adaptation Under Reduced Oxygen Tension, Am. J. Physiol. **127**:37-50, 1939.

9. Evans, J. N., and McFarland, R. A.: The Effects of Oxygen Deprivation on the Central Visual Field, Am. J. Ophth. **21**:968-980, 1938.

10. Seitz, C. P.: Alterations in Critical Frequency Under Conditions of Reduced Oxygen Tensions, Arch. Psychol., 1940, no. 259.

application of strychnine to the conjunctiva is to increase retinal sensitivity. When administered under conditions of altitude which ordinarily depress retinal sensitivity, strychnine sustained the function on a level that was nearly normal. The data obtained in that study led to the conclusion that strychnine (a neural stimulant) seems to diminish or cancel the effect due to oxygen deprivation (a neural depressant). The data given in the report offer rather definite evidence concerning the primary importance of neural mechanisms in producing variations in critical flicker frequency [11] under conditions of oxygen deprivation and administration of strychnine. The part played by photochemical change was not strictly determined in this research, though it is expected to be minor.

PROBLEM

The purpose of the present study was to extend the aforementioned research through investigation of the changes in the visual fields at an altitude of 17,500 feet (5,250 meters) after direct application of strychnine to the eye. In addition, the results of this study should be of considerable theoretic significance for a sound understanding of the nature of the angioscotoma.

MATERIAL AND METHOD

Angioscotometry was used to measure the central visual fields. The name "angioscotoma" is used to indicate a "defect of the visual field originating from the blindspot of Mariotte and related in form to the pattern of distribution of the retinal vessel tree." After extended research it has been suggested that these shadows arise through modifications of the functions of the retinal perivascular spaces.[12]

Technic of Angioscotometry.—The area of the scotoma is determined by a technic perfected by Evans,[13] which permits a statement of the field defect in such form that the results may be qualitatively and quantitatively examined.

The Lloyd stereocampimeter and charts were used. Monocular fixation was employed throughout the experiment. The subject was comfortably seated and relaxed before the mapping was started. The disappearance of the test object was indicated by tapping. The diameter of the test object used was 0.55 mm. The blindspot of Mariotte was then outlined. After this the two main superior angioscotomas were plotted, care being exercised to move the object at right angles to the defect.

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11. The point at which alternate retinal stimulation is just rapid enough to create a sensation comparable to that of a continuous and smooth surface.

12. Evans, J. N.: A Preliminary Report on the Retinal Vessel Scotoma, Am. J. Ophth. **9**:118-119, 1926; Angioscotometry, ibid. **9**:489-506, 1926.

13. Evans, J. N.: Clinical Scotometry, New Haven, Conn., Yale University Press, 1937.

Oxygen Apparatus.—All the experiments were carried out in a Barach portable oxygen chamber.[14] This chamber consists of an angle iron frame 7 by 7 by 8 feet (2 by 2 by 2.4 meters) covered with rubberized fabric. An air-conditioning unit maintained comfortable temperature and humidity (temperature, 65 to 70 F.; humidity, 40 to 50 per cent). An altitude of 17,500 feet was simulated by running nitrogen into the chamber and diluting the air. Samples of the chamber air were taken after the ascent and subsequently analyzed on the Haldane, Henderson and Bailey gas analysis apparatus. None of the simulated ascents deviated more than the equivalent of 500 feet (150 meters) from the desired altitude.

Subjects.—Four male students free from known ocular and systemic defects as determined by ophthalmologic and medical examinations served as subjects. The age range was 21 to 26 years.

Procedure.—The subjects were examined individually and rested ten minutes before any measurements were made. During the rest period they were acquainted with the apparatus and the manner of making the response; blood pressures and pulse rates were recorded. A further period of relaxation (five minutes) was allowed before the first maps, called control maps, were plotted. Both eyes were mapped. After this 3 drops[15] of a 1 per cent solution of strychnine sulfate was applied to the conjunctiva of one eye and, as a control, 3 drops of sterile water to the other. Maps of both eyes were plotted at intervals of fifteen minutes until the effect of the drug had worn off. The blood pressure and the pulse rate were recorded immediately after each mapping. Care was exercised to avoid all influences which are known to affect the angioscotoma.[16]

At the next experimental period the same general procedure was followed. Immediately after completion of the control maps the ascent to the simulated altitude of 17,500 feet was made. Maps were plotted at the end of the ascent, which took fifteen minutes, and again fifteen minutes later. Three drops of strychnine sulfate solution (1 per cent) was then applied to one eye and water to the other, and maps were plotted at fifteen minute intervals.

RESULTS

The results are presented in the charts and tables. The maps plotted during the first experimental period (sea level) clearly show that the area of the scotoma decreased after the administration of strychnine. The maps plotted during the second experimental period show that oxygen deprivation equivalent to that encountered at an altitude of 17,500 feet caused a marked increase in the scotoma. After the administration of strychnine to one eye a pronounced decrease in the blind area was apparent, while in the untreated eye no such change occurred.

14. Barach, A. L.: An Oxygen Chamber Simplified in Design and Operation, J. A. M. A. **97**:390-391 (Aug. 8) 1931.

15. Applied at one minute intervals; the puncta were closed.

16. Evans and McFarland.[9] Evans.[13]

The blind area of each eye was measured in square inches with a planimeter.[17] The data are presented in tables 1 and 2 and lend quantitative support to the changes qualitatively apparent from the maps. Examination of table 1 shows the average area of the control maps for

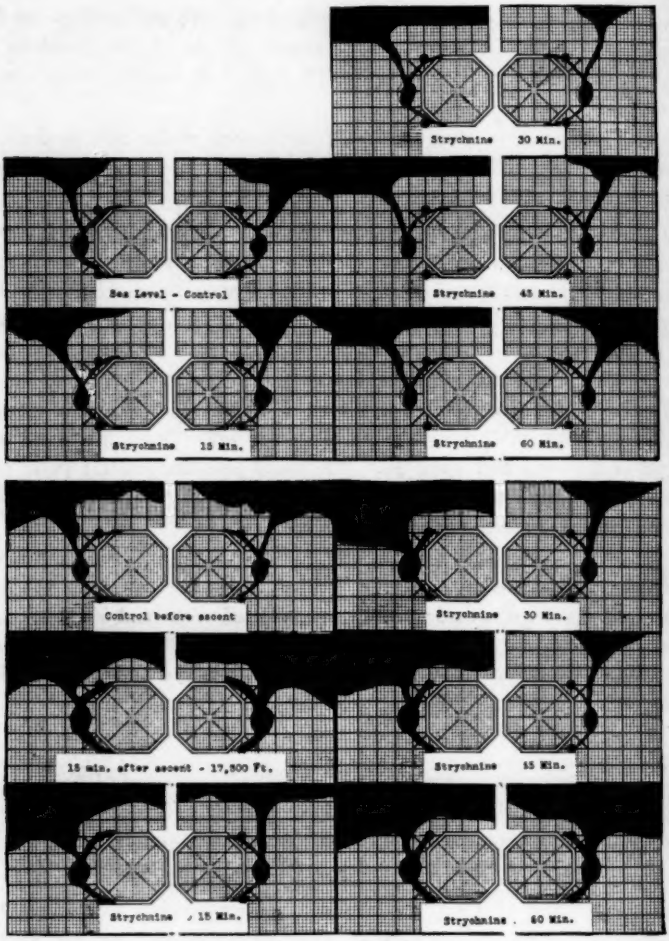

Chart 1.—Maps of the angioscotomas of subject K. R., showing the effects of 3 drops of strychnine in the right eye in counteracting the effect of a simulated altitude of 17,500 feet (5,250 meters). A 0.55 mm. test object was used.

4 subjects to be 1.23 square inches (7.8 sq. cm.) for the right eye and 1.15 square inches (7.3 sq. cm.) for the left eye. The bold face figures of the

17. This differs from Evans' technic in that the measurement is a relatively accurate determination of the blind area, whereas his is but an approximation.

table represent the average blind area of the strychninized eyes and are to be compared with the adjacent figures, which give the mean area of the untreated eyes. The average area for successive fifteen minute periods was 1.35, 1.08, 1.42 and 1.35 square inches (8.6, 6.9, 9 and 8.6

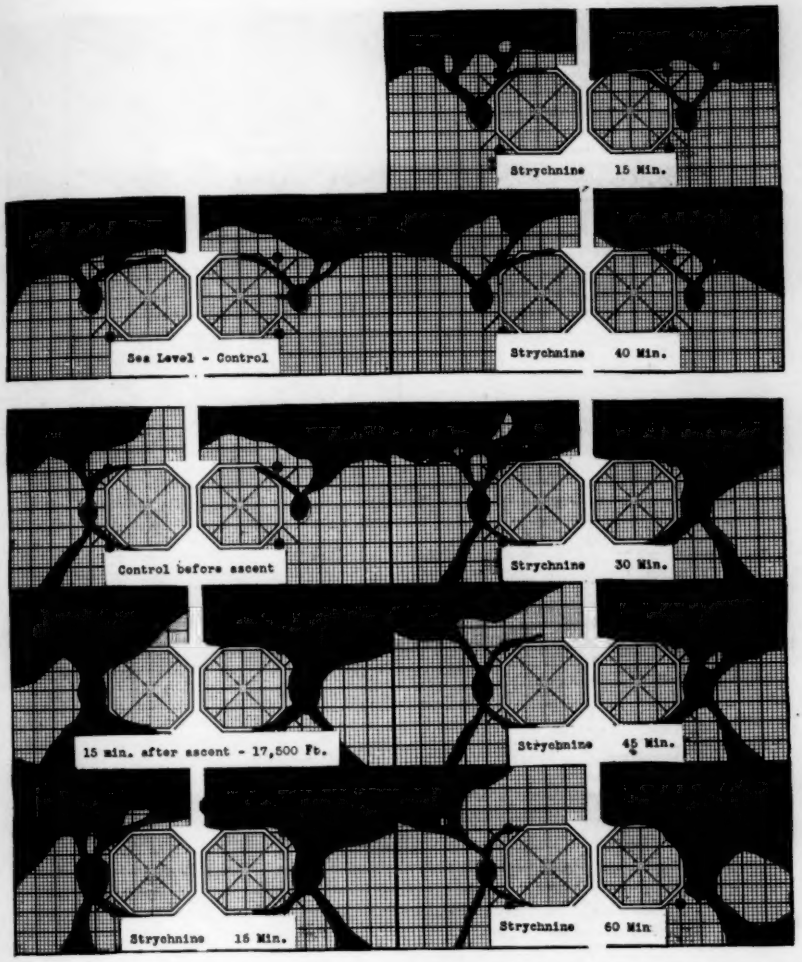

Chart 2.—Maps of the angioscotomas of subject C. S. Strychnine was applied to the left eye. A 0.55 mm. test object was used.

sq. cm.) for the control eye and 0.88, 0.47, 0.89 and 1.09 square inches (5.6, 3, 5.7 and 7 sq. cm.) for the treated eye.

Columns 1 and 2 of table 2 show the average scotoma at sea level and fifteen minutes after ascent to 17,500 feet. It is to be noted that the average scotoma is nearly 100 per cent greater under these conditions.

The bold face figures as in table 1 show the average blind area of the strychninized eye and are to be compared with the adjacent figures, which give the average blind area of the control eye. The average area for successive fifteen minute periods is 2.26, 2.19, 2.18 and 2.41 square

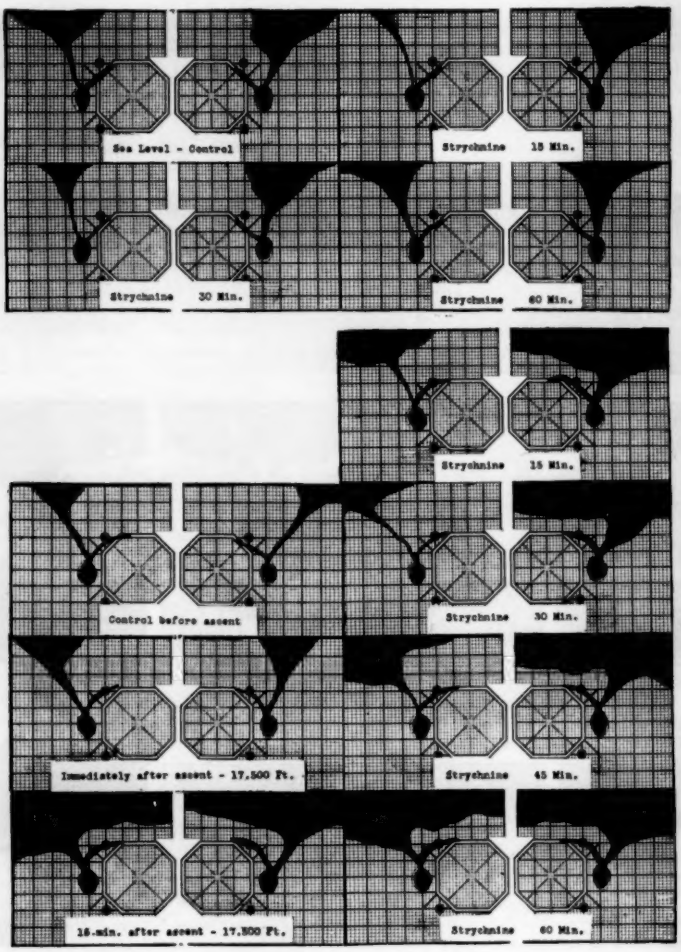

Chart 3.—Maps of the angioscotomas of subject O. M. Strychnine was applied to the left eye. A 0.55 mm. test object was used.

inches (14.4, 14, 13.9 and 15.4 sq. cm.) for the control eye and 1.28, 0.95, 1.47 and 1.63 square inches (8, 6, 9.4 and 10.4 sq. cm.) for the strychninized eye. These values approximate the normal values obtained at sea level.

The tables also show that the effect of strychnine in decreasing the scotoma was produced within the first fifteen minutes of its administration. The maximum effect of the drug was experienced at approximately sixty minutes.

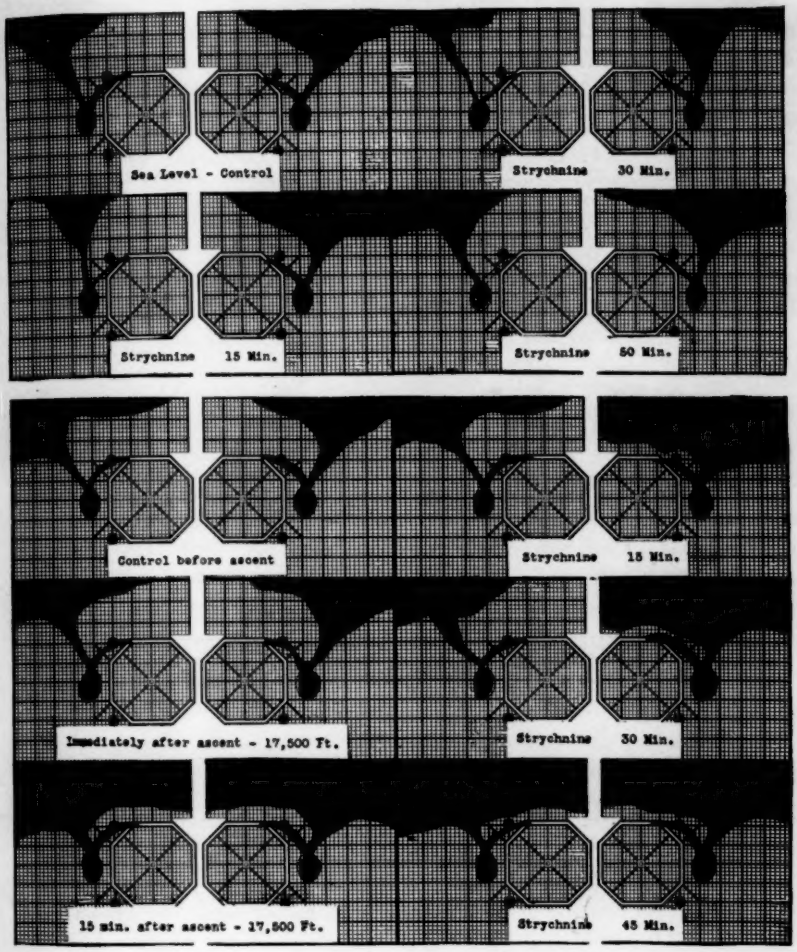

Chart 4.—Maps of the angioscotomas of subject C. O. Strychnine was applied to the left eye. A 0.55 mm. test object was used.

There were no marked or consistent vascular changes (table 3). No general systemic involvement resulting from administration of strychnine was subjectively reported or otherwise noted. The suggested local action of the drug is supported by the consistent results in the treated eye and the lack of change in the control eye.

TABLE 1.—*Average Blind Area (in Square Inches) for the Right and the Left Eye at Sea Level With and Without Strychnine*

Subject	Without Strychnine 15 Minutes		With Strychnine							
			15 Minutes		30 Minutes		45 Minutes		60 Minutes	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
C. S. (OS)*	2.06	2.08	2.48	1.82	....	....	2.49	1.55	....	....
K. R. (OD)†	0.90	1.00	0.95	0.69	1.32	0.46	1.30	0.65	1.35	1.09
O. M. (OS)	0.87	0.75	0.72	0.50	1.00	0.36	0.76	0.46	....	....
C. O. (OS)	1.09	0.79	1.27	0.52	0.93	0.60	1.14	0.90	....	....
Mean	1.23	1.15	1.35	**0.88**	1.08	**0.47**	1.42	**0.89**	1.35	**1.09**

* Strychnine in left eye.

† Strychnine in right eye, but placed in left column for purposes of comparison.

TABLE 2.—*Average Blind Area (in Square Inches) for the Right and the Left Eye at Sea Level and at Altitude With and Without Strychnine*

Subject	Sea Level (Before Ascent)		15 Minutes After Ascent		With Strychnine							
					15 Minutes		30 Minutes		45 Minutes		60 Minutes	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
C. S. (OS)*	1.95	1.45	2.62	2.70	2.40	2.30	2.70	1.95	2.70	1.33	3.00	1.40
K. R. (OD)†	1.44	1.20	2.14	2.19	2.56	0.65	2.12	0.46	2.25	2.18	....	....
O. M. (OS)	0.45	0.50	1.53	2.05	1.82	1.09	1.80	0.40	1.75	1.02	1.82	1.87
C. O. (OS)	1.04	1.29	2.02	2.75	2.25	1.08	2.14	0.91	2.03	2.14	....	....
Mean	1.22	1.11	2.08	**2.27**	2.26	**1.28**	2.19	**0.93**	2.18	**1.47**	2.41	**1.63**

* Strychnine in left eye.

† Strychnine in right eye, but placed in left column for purposes of comparison.

TABLE 3.—*Pulse Rate and Blood Pressure at Sea Level and at Altitude Both With and Without Strychnine*

Subject	Sea Level						Altitude		
	Control			Strychnine			Strychnine		
		Blood Pressure			Blood Pressure			Blood Pressure	
	Pulse Rate per Min.	Systolic, Mm. Hg	Diastolic, Mm. Hg	Pulse Rate per Min.	Systolic, Mm. Hg	Diastolic, Mm. Hg	Pulse Rate per Min.	Systolic, Mm. Hg	Diastolic, Mm. Hg
K. R.	82	105	67	82	106	65	91	113	64
C. O.	81	120	70	84	121	78	93	110	69
O. M.	81	120	67	81	117	69	90	103	56
C. S.	..	...	..	..	...	..	..	...	..
Mean	81.3	115	68	82.3	114.7	70.7	91.3	108.7	63

COMMENT

Under the conditions of these experiments it was found that the scotoma under conditions of oxygen deprivation equivalent to that encountered at an altitude of 17,500 feet is restored to normal through the direct application of 3 drops of a 1 per cent solution of strychnine sulfate to the conjunctiva. It has been reported by Evans [13] that change in the size of the scotoma may arise from a variety of causes. Every precaution was observed, however, to control these factors. Changes in total pressure were avoided by working at sea level, and, as has been observed, the vascular changes were insignificant. In addition, all the subjects had had previous experience as observers in the oxygen chamber, and hence the probability of disturbing emotional effects was slight. Evans and McFarland,[9] observing the same precautions, concluded that the widening of the blind areas results not from incidental systemic changes accompanying oxygen deprivation (such as apprehension or changes in blood pressure) but rather from an insufficiency of oxygen reaching the retina in the regions corresponding to the defect. Evans [13] has suggested that the locus of the effect is at the synapse. Evidence with respect to such an interpretation has been reported by Rosenthal,[18] who found that a relatively high concentration of oxygen reduces the size of the blind areas. Changes in flicker frequency associated with oxygen deprivation lend further support to this hypothesis.

The results of this study, indirect and hardly crucial, bear on this point. Classically, strychnine [19] is thought of as a neural stimulant, and in this study, as in a previous study by one of us (Seitz [10]), the effect of strychnine counteracted the effect of oxygen deprivation, a neural depressant. Of particular interest was the local effect of the drug, which was clearly shown by the results for the treated and the untreated eye. This evidence, supported by the absence of vascular and systemic change (table 3), suggests that the widening of the scotoma is to be attributed to a change in function of the retinal structures occurring as a consequence of oxygen deprivation. Whether this change is vascular or neural was not directly determined by this study, though it is thought likely, in view of the pharmacologic effects of strychnine, that the action of oxygen deprivation is directly on the neural tissue; in this sense the study bears out Evans' original hypothesis. The soundness of this conclusion will be subjected to experimental test in the near future.

18. Rosenthal, C. M.: Changes in Angioscotomas Associated with Inhalation of Oxygen, Arch. Ophth. **22**:385-392 (Sept.) 1939.

19. Starling, E. H.: Principles of Human Physiology, ed. 6, Philadelphia, Lea & Febiger, 1933, p. 1122.

It is interesting to speculate on the reports of other researches. In both this study and that of Evans and McFarland,[9] oxygen deprivation had no effect on the macular region of the eye. If this is so, any theory involving synaptic dysfunction is incomplete if not untenable, for it is well known that this region is abundantly supplied with synaptic structures. Changes in flicker frequency for central fixation [10] as well as changes in visual acuity [20] under conditions of oxygen deprivation show definite central impairment. It appears, therefore, that the difficulty is not with the hypothesis but rather with the conditions set by the experiment. If the angioscotoma results from synaptic dysfunction, then, it remains to be shown under appropriate conditions that central function is also impaired or that the region under consideration (macular, perimacular) is protected from oxygen deprivation by some supplementary mechanism. This factor is now under investigation.

The implications of this study are not only of theoretic interest in relation to the role of oxygen in visual function; certain practical applications are also apparent. It has previously been shown [21] that exposure to a simulated altitude of 16,000 feet (4,800 meters) for a little more than one hour causes a depression in psychologic functions which may be counteracted to some extent by 10 mg. of benzedrine sulfate. In this study we have been able to show that a 1 per cent solution of strychnine sulfate also counteracts the effect of oxygen deprivation. No suggestion is made that strychnine be used regularly to increase visual efficiency, but it may be useful in emergency situations, such as flying at high altitudes for short periods. The same may be said for the use of amphetamine and ephedrine. Clinically, there is also some possibility of its use in recovery from temporary blindness consequent on poor retinal circulation.

SUMMARY AND CONCLUSIONS

The eyes of 4 subjects were carefully plotted at sea level and under altitude conditions by the method of angioscotometry. Maps were again plotted under similar conditions, except that 3 drops of a 1 per cent solution of strychnine sulfate was applied to one eye and 3 drops of water to the other. It was found under the conditions of this experiment that:

1. The scotomas on successive measurements were consistent.
2. Oxygen deprivation caused a widening of the defect.
3. Macular vision remained unaffected.

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20. McFarland, R. A., and Halperin, M. H.: The Relation Between Foveal Visual Acuity and Illumination Under Reduced Oxygen Tension, J. Gen. Physiol. **23**:613-630, 1940.

21. Seitz, C. P., and Barmack, J. E.: The Effects of Ten Milligrams of Benzedrine Sulphate and Low Oxygen Tension on the Span of Attention for Letters, and Other Factors, J. Psychol. **10**:241-247, 1940.

4. Strychnine administered at sea level caused a marked narrowing of the scotoma in the treated eye. No such change was apparent in the untreated eye.
5. Strychnine administered in the same way counteracted the widening of the scotoma resulting from 17,500 feet of altitude.
6. No relation between minor variations in blood pressure, pulse, pupillary area and the size of the scotoma was apparent.
7. It is suggested that more elaborate pharmacologic experiments be made before conclusions are drawn as to the mechanisms of the angioscotoma.

THE "FOSTER KENNEDY" SYNDROME

A FOOTNOTE TO OPHTHALMOLOGIC HISTORY

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More than thirty years ago Leslie Paton began to publish, in *Brain*, in the *Transactions of the Ophthalmological Society of the United Kingdom*, and as monographs, a series of studies on pathologic changes in the optic nerve in relation to intracranial lesions, tumors of the brain and allied conditions. Much of the material came from the pathologic laboratory and from the wards of the National Hospital for Nervous Diseases —Queen Square, as it was known to neurologists—and concerned patients admitted to the service of Sir William Gowers, Mr. Gordon Holmes and others. This interesting and instructive research, based on a wealth of clinical observation as well as on histologic data, dealt with papilledema, atrophy of the optic nerve and neural changes in disseminate sclerosis and in tabes. The papers presented an unusual amount of well digested evidence on the ophthalmoscopic appearance, the pathologic mechanism and the histologic picture of papilledema. Paton discussed the "star" figure at the macula seen in some cases of this change in the disk and noted that, in contradistinction to the classic form seen in what was formerly called Bright's retinitis, it is really a fan, an incomplete star. He explained this forme fruste as being due to edema, spreading from the nerve head in choked disk and blocked by the tissues in the macular region, notably Müller's supporting fibers. In addition, there are valuable notes on the relation of the tumor site to the laterality and to the severity of the changes in the nerve head, the mechanism of choked disk in disseminate sclerosis and much else, with a complete review of the literature, and due credit was given to previous authors. Much of Paton's work was done in collaboration with Sir William Gowers and was referred to and checked up by him. One of Paton's histologic preparations—as he himself mentioned more than once—was used by Gowers to illustrate a lecture on simple atrophy due to direct pressure on the nerve by a tumor of the brain. Paton repeatedly drew attention to the fact that papilledema when bilateral might differ greatly in the degree of intensity in the two eyes and that it was frequently seen in one eye only, for a time or even permanently, i. e., until death intervened or the cause of the choked disk was removed by intracranial operation. Also, a simple atrophy might later develop in the apparently

unaffected eye. Paton stressed this syndrome in more than one passage. He reported a case in which a tumor of the right frontal lobe compressed the right optic nerve and chiasm.[1] There was left hemianopia with fair central vision in the left eye, but central vision was absent in the right eye. His description reads as follows:

> The right optic disk was normal in appearance. . . . The left optic disk showed intense optic neuritis [2] . . . and a swelling of two dioptres. In this case, then, the pressure of the tumour gave rise to blindness in the right eye, though no primary atrophy had, at the time of death, shown itself in the right disk. In another case . . . however, there was a marked primary atrophy in the left eye with an intense neuritis in the right. Post-mortem examination revealed a large frontal tumour. . . . The left nerve was directly pressed on by the tumour.
>
> These cases show that direct pressure on the intracranial portion of the nerves or on the chiasma may cause loss of vision and pressure atrophy without causing optic neuritis.

On page 77 of the same article he cited these cases and referred to his "true explanation of the non-development of the neuritis" in one eye.

Two years later this syndrome, first described, analyzed and explained by him, was mentioned again.[3] In his presidential address before the Royal Society of Medicine in November 1930, Paton [4] stated:

> I called attention many years ago to the importance, from a localizing point of view, of the appearance of an atrophy on one side and a papilloedema on the other side. Almost the last lecture that Sir William Gowers gave at Queen Square [later the same year] was devoted to a case of this kind of which I had cut the sections.[5] Subsequently Kennedy gathered together several cases illustrative of the value of this phenomenon as indicating the location of the pressure.

A final reference is found as Paton looked backward in a paper on papilledema and optic neuritis read before the Section on Ophthalmology of the American Medical Association on June 12, 1930.[6] He stated

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1. Paton, L.: A Clinical Study of Optic Neuritis in Its Relationship to Intracranial Tumors, Brain **32**:68, 1909.

2. In 1908 the term optic neuritis was still used (Paton, L.: Papilledema and Optic Neuritis: A Retrospect, Arch. Ophth. **15**:1 [Jan.] 1936). The term papilledema was first recommended by Parsons (1908).

3. Paton, L.: The Pathology of Papilledema: A Histological Study of Sixty Eyes, Brain **33**:420, 1911.

4. Paton, L.: President's Address: Classification of Optic Atrophies, Proc. Roy. Soc. Med. **24**:25, 1930.

5. ". . . but all Gowers did was to use these specimens as a text to expound in more detail what I had already stated in a paper in *Brain*" (Paton, L.: Personal communication to the author, March 16, 1936).

6. Paton, L.: Papilledema and Optic Neuritis: A Retrospect, Arch. Ophth. **15**:1 (Jan.) 1936.

that he had first gone to Queen Square as an assistant to Marcus Gunn in the year 1902.

> At that time Gowers, Ferrier, Horsley, Buzzard, Risien Russell and others were still actively working there. Hughlings Jackson was still a regular visitor to the wards and a source of inspiration to all his juniors. . . . At the end of 1908 I had a postmortem opportunity of confirming my belief that a tumor . . . on the under surface of the frontal lobe would cause atrophy of the collateral nerve and papilledema on the opposite side. This case is of some historical interest since it formed the subject of the last public lecture that Sir William Gowers gave. . . . Gowers, in his lecture, said: "Any case which presents this condition [i. e., atrophy in one eye and papilledema in the other] will probably warrant the same diagnosis." In his own words: "You may assume that the optic neuritis produced by an ordinary intracranial tumour is always produced in both eyes." He quotes the one exception: "In this the monocular neuritis from cerebral disease having the symptoms of a tumour was confined to the right eye, but . . . the left was artificial!"

Paton noted that the tumor had blocked the left optic foramen and added that this thesis was developed at greater length by Foster Kennedy.[7]

The historical interest invoked by Paton also applies, in my opinion, to priority in the discovery, analysis and explanation by him of what is generally referred to as the Foster Kennedy syndrome. I do not know whether Gowers in the aforementioned lecture or elsewhere gave credit to Paton. Be that as it may, there is no reason why credit should continue to be withheld from one to whom it is so justly and richly due and who himself cited so generously many other workers in this field.

An instance of this silence as to Leslie Paton's pioneer work is the chapter by Rönne on papillitis in the "Kurzes Handbuch der Ophthalmologie" [8] in which credit for the syndrome is given to America, via Foster Kennedy. There is no mention of Paton either in the text or in the Bibliography.

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7. Kennedy, F.: Retrobulbar Neuritis as an Exact Diagnostic Sign of Certain Tumors and Abscesses in the Frontal Lobes, Am. J. M. Sc. **142**:355, 1911.

8. Rönne, H., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 5.

Clinical Notes

A SIMPLE INSTRUMENT FOR TESTING VERTICAL MUSCLE BALANCE AT READING DISTANCE

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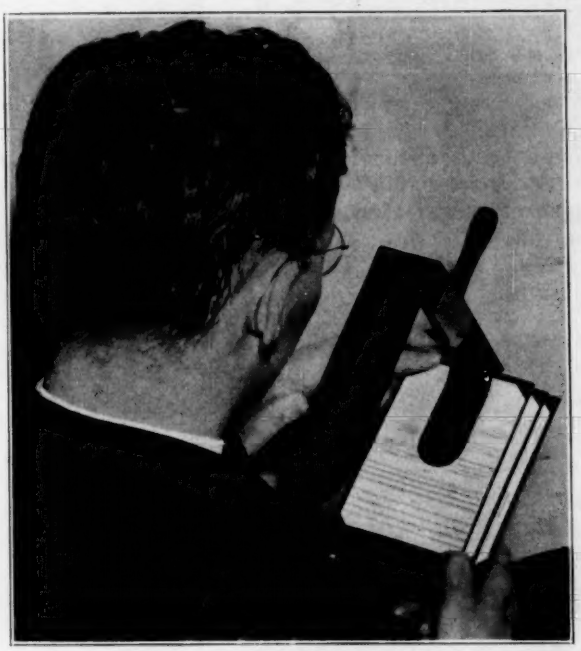
The instrument consists of a metal divider 5 cm. wide, which when slid over the edge of a reading card, as in the accompanying illustration, projects about 20 cm. in front of the card and divides the print into two



Instrument for testing vertical muscle balance at reading distance.

equal columns. The width of the divider is such that it obscures the left column from the patient's right eye, so that the right eye sees only the right column. The left eye likewise sees only the left column. If any hyperphoria is present the column of print seen by the hyperphoric eye will appear lower than that seen by the opposite eye. The amount of prism base down before the hyperphoric eye which will bring both columns to the same level is the measure of the amount of hyperphoria present under normal reading conditions.

The first advantage of a test with this instrument is that it can be applied when the patient is holding the reading card at the distance and in

the position to which he is accustomed. It is thus possible to correct his hyperphoria under the conditions in which he does his close work. This is particularly important when the hyperphoria is due to inequality in the prismatic effects of the lenses required by the patient, for in this case the degree to which he looks down when in his natural reading position determines the amount of the phoria.

The second advantage is the low degree of fusion tendency. When the Maddox rod test has given normal results for the reading distance, the test here described has frequently shown an amount of hyperphoria which required correction, i. e. as much as 1 D. This of course is due to the fact that many patients can fuse the light and the line in the Maddox test.

This test has been used in two hundred refractions and has been found entirely satisfactory. It is of great help in deciding whether a prism should be used in the patient's bifocal lenses.

DESCRIPTION

The instrument was devised by a Reading optician, Mr. R. C. Vulkoff, for use in correcting prismatic effects of unequal lenses under actual reading conditions. It consists simply of a metal strip 5 cm. wide with two right angle bends, as illustrated. The two long sides are each 21 cm. in length. The short end, which is placed behind the reading card, is 6 cm. in length. Another strip of metal 5 cm. wide and 10 cm. long is soldered in front of the short strip, the two forming a clip which fits over the upper edge of the card. The handle may be added for convenience but is not essential.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

THE DIVERGENCE IMPULSE

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The purpose of the following comments is to communicate some reflections on the part played by a divergence impulse in binocular coordination and in the clinical entity known as divergence excess.

Duane [1] was the first to suggest that divergence excess is an important anomaly of binocular function. In his series of essays giving a new classification of motor anomalies of the eyes he divided extraocular muscle functions into hypokinesis and hyperkinesis. In the category of hyperkinesis is divergence excess, or overaction of divergence. It is characterized by the following signs: There is exophoria for distance, which is usually marked, that is, more than 4 prism diopters, with a noticeable deviation out behind the screen. The associated lateral movements are normal. Diverging prisms of more than 9 prism diopters can be overcome, while divergence of 6 to 8 prism diopters was considered normal by him. Prism divergence is usually proportionate to the exophoria but is sometimes disproportionately larger. Adduction is normal in uncomplicated cases. Often a spontaneous crossed diplopia is observed. Unless convergence insufficiency also exists, muscle function for near vision is normal; that is, the exophoria is less for near vision than for distance, and the near point of convergence is at normal distance. Divergence excess may have a primary origin or may be secondary to divergence insufficiency. The primary form occurs not infrequently as an uncomplicated condition, but much more often it is associated with a vertical deviation or with a consecutive divergence insufficiency. It may also be associated with convergence excess. Duane observed several instances in which exophoria for distance associated with high divergence power (divergence power is a term used by him) had an excessive power of convergence for near vision with actual esophoria for near vision or at least exophoria which was smaller for near than for distant vision. The symptoms of divergence excess Duane held to be slight. The most troublesome, he stated, are those due to an

1. Duane, A.: A New Classification of the Motor Anomalies of the Eye, Based on Physiological Principles, Ann. Ophth. **6**:247, 1897.

associated convergence insufficiency. Headache and asthenopia may occur.

Writing in 1927, Dunnington [2] also discussed divergence excess. Basing his opinion on the belief that for near viewing the power of divergence is in a state of relaxation and convergence is stimulated and that for distant viewing there are relaxation of convergence and active stimulation of divergence, he concluded that in a case of pure divergence excess the following manifestations are present:

Marked exophoria for distance, 5 to 40 degrees
Excess prism divergence
Normal prism convergence
Normal muscle balance at 13 inches (33 cm.)
Normal near point of convergence
Lateral movement of eyes in and out, normal in extent and comitant
Diplopia, if present, not increasing right or left

He expressed the belief that divergence excess is to be differentiated from convergence insufficiency and from insufficiency of an adductor muscle. The former of these possibilities is characterized by normal findings for distance and marked exophoria at 13 inches (33 cm.). If an exophoria is greater at 20 feet (6 meters) than at 13 inches, it is primarily due to divergence excess. Divergence excess may become complicated with secondary divergence insufficiency, and it may also be secondary to convergence insufficiency. Duane stated that divergence excess appears in a primary and a secondary form. The exact cause of the primary form is not understood. In childhood it is uncomplicated, but later it is usually associated with convergence insufficiency. Among the symptoms he mentioned headache and asthenopia and stressed the fact that the eyestrain is of the panoramic type. The patients usually abhor crowds. Some have no symptoms except that they are unable to sustain near work for long periods because of secondary convergence insufficiency. Even gastric symptoms are known to predominate in some patients.

In 1929 Berens, Hardy and Stark [3] reviewed the records of 1,100 of their patients and found that 1 to 2 per cent of all the total number had divergence excess. They defined divergence excess as that form of ocular muscle imbalance which exhibits exophoria more marked when the gaze is directed into the distance than when it is adjusted for near

2. Dunnington, J. H.: Divergence Excess: Its Diagnosis and Treatment, Am. J. Ophth. **56**:344, 1927.

3. Berens, C.; Hardy, L., and Stark, E.: Divergence Excess, Tr. Am. Ophth. Soc. **27**:263, 1929.

vision, combined with normal prism convergence and near point of convergence and excessive ability to overcome diplopia caused by prisms base in.

Bielschowsky expressed a different view of divergence excess; in fact, he doubted its existence until he observed a patient with a striking clinical picture which he was able to watch for eleven years. He described the clinical course in great detail in a German journal [4] and again more briefly made it the basis of a discussion on divergence excess in the ARCHIVES in 1934.[5] Here he stated that Duane and Dunnington did not sufficiently stress the importance of an anomalous position of rest dependent on purely mechanical conditions as one of the most important factors in the causation of divergent strabismus. Divergence excess, on the other hand, is an anomaly of nervous origin. His patient was a neuropathic woman who in 1918, at the age of 22, noticed impairment in vision. He did not see her until four years later but then was able to observe her at intervals for eleven years. Her chief difficulty was myopia produced by a spasm of accommodation. This spasm of accommodation was ascribed to a convergence impulse which was necessary to overcome exophoria. She had an abnormal range of divergence. This was, however, not dependent on a corresponding divergent position of rest or the result of insufficiency of convergence. By an advancement of both internal rectus muscles he made the patient orthophoric, and the near point of convergence was normal. Before operation the convergence impulse associated with accommodation had been just enough to bring about parallelism of the axes of the eyes. After the exophoria had been corrected, actual convergence was produced by the same impulse.

The abnormal range of divergence and the relative divergence at reading distance must have been derived from an abnormal irritability of the center controlling divergence and therefore must have been of nervous origin.

Dunnington, in a discussion of this paper, pointed out that Bielschowsky seemed to be in accord with Duane on many points; namely, the existence of a divergence center in the presence of a divergence innervation antagonistic to the convergence innervation and the innervational origin of divergence excess. The only diversity of opinion, he said, seemed to concern the role that divergence excess plays in the production of divergent strabismus.

Although these statements are true, they tend to minimize the differences in point of view between Duane and Bielschowsky. The latter based his diagnosis on a qualitative analysis of several manifestations, the most important of which is the production of myopia by the accommoda-

4. Bielschowsky, A.: Exophorie und "Divergenzexzess," Klin. Monatsbl. f. Augenh. **92**:11, 1934.

5. Bielschowsky, A.: Divergence Excess, Arch. Ophth. **12**:157 (Aug.) 1934.

tive effort which accompanies the convergence impulse that is necessary to counteract the divergence. Duane, on the other hand, based his judgment on variations in quantitative measurements of various functions, namely, exophoria, divergence and convergence. These are names for clinical phenomena or manifestations which are not directly observable by inspection but rather describe the behavior of a pair of eyes under certain conditions which are arranged in the form of a test.

THE TESTS

In all of the tests it is assumed that one is testing functions of a mechanism of binocular coordination and that the integrity of the actual peripheral motor mechanism has been established by suitable tests of the ocular movements.

Exophoria is commonly measured by means of the screen test and the Maddox rod. The former is the more reliable, because the patient is less tempted to bring about fusion of the images. With both tests one strives to measure the relative position of the optic axes in the presence of all stimuli except the fusion impulse.

In the screen test this is accomplished by screening one eye so that the other alone is allowed to see the object of fixation. The covered eye presumably assumes that position which it takes in absence of the fusion urge. The screen is then shifted to the other eye. The formerly covered eye must now make a movement to bring an image of the object of fixation onto its fovea. By placing prisms of various strengths before this eye until one is found that makes movement of the eyeball unnecessary, its angular position in relation to the fixing eye is measured. In the Maddox rod test the two eyes are allowed to fix a small light simultaneously, but a series of rods of red glass is placed before one eye so that the two images become too dissimilar to be readily fused. The angular relative position is measured with that prism which brings the two images together. Both tests are made with the focusing mechanism adjusted for distant as well as for near gaze—usually 5 meters and 33 cm. respectively. It is of the utmost importance that the distance for near vision be actually measured. An error of a few centimeters will completely change the value, as will be seen in the discussion of the interpretation of the tests in a later paragraph.

The Maddox wing test is a convenient automatic screen test. It is used at 33 cm.

Divergence is measured by placing before one eye in the abducting position the maximum prism with which binocular single vision can be maintained. Convergence can be similarly measured with an adducting prism. It may also be measured by determining the smallest distance from a line traversing the centers of rotation at which a small object

can be fixed by the two eyes simultaneously. If the interpupillary distance is known, the angle of convergence can be approximately calculated by means of Duane's formula:

$$\text{angle of convergence} = \frac{\text{interpupillary distance} \times 50}{\text{near point of convergence}} + 3^\circ$$

If the latter method is used, the accommodation impulse normally associated with convergence need not be held in abeyance; hence, convergence so measured is usually found to be slightly greater than when a prism is used in conjunction with a distant light.

Accommodation is judged by its amplitude, or range. This is conveniently stated in diopters to express the amount of increase of refractive power possible to the eye. In an emmetropic eye the greatest distance of effective focus is infinity and the focal adjustment necessary is zero. The near point of accommodation is found by determining the shortest distance at which a fine black line on black paper can be clearly seen. If referred to a point 13 mm. anterior to the corneal apex, the anterior focal point of the eye, the accommodative change in the eye may be expressed in terms of the dioptic strength of a lens whose focal length equals the distance found.

Significance of the Values Determined by the Tests.—It is on difference from the normal of the aforementioned measurements that recognition of divergence excess depends.

When an author discusses a disorder of ocular coordination, he must accept explicitly or by implication the existence of a normal order of function. There is no unanimity of opinion as to the details of the order, because its mechanism is not understood in detail. At least three degrees of complexity of integration are conceivable, and an author tacitly grants one of them as approximately true when he discusses problems of binocular coordination.

The first, and simplest, degree implies that one believes that impulses are constantly transmitted to the individual ocular muscles to bring about tonic postural adjustments and that through the agency of the afferent impulses controlled by sensory impressions corrections in the interest of binocular single vision are made.

A similar mechanism exists but has a greater degree of complexity of organization because the corrective movements are not brought about by impulses directly to the several muscles but by two highly integrated intermediate centers for convergence and divergence. They function reciprocally but only under visual control in the interest of fusion.

A third degree of integration is conceivable. The integrated functional units for divergence and convergence could be in constant cooperation to bring about a position of the optical axes in relation to each other which is known as phoria and exists without afferent visual control.

Of course, none of these mechanisms is known in detail, but the utterances of discussants of problems concerning ocular muscle function betray acceptance (more often than not unexpressed) of a scheme of organization roughly corresponding to one of them.

It will be one of the functions of the remainder of this review to point out what facts are known and to state explicitly how some of the accepted conceptions are related to the implied assumptions in the hope that the procedure will keep the facts perspicuous for use in diagnosis of the ailments of patients as well as in the construction of conceptual abstractions. The following brief survey of the general physiology of ocular muscle control, which precedes the discussion, is not offered as a blueprint on the basis of which the details of the mechanism of divergence, convergence, phoria and similar phenomena may be explained. It is presented rather to give pause to any who are tempted to too facile generalizations and unwarranted conclusions about the mechanisms of binocular coordination.

THE GENERAL PHYSIOLOGY OF THE OCULAR MOTOR SYSTEM [6]

The exquisitely controlled movements of the eyeballs necessary to create and maintain binocular coordination are brought about by the extraocular muscles. These muscles are controlled by the motor nerves, whose nuclei are in the brain stem. The nuclei are in turn stimulated to complexly integrated activity through supranuclear fiber bundles whose impulses originate in the cortical centers.

When the eye is fixed, nervous impulses are constantly sent down the nerves, producing a contraction of the antagonistic muscles known as tonus. When the eye moves, increased contraction of one muscle is associated with a relaxation of its antagonist adequate to bring about smooth and delicately controlled change of position, according to the principle of reciprocal innervation. For this purpose each muscle functions in unit bundles of many individual fibers—one hundred and fifty or more—each innervated by one nerve fiber to whose excitation it responds entirely or not at all. This is so because the nerve fiber behaves according to the "all or none" principle. The reason why there are many muscle fibers for each nerve unit rather than one correspondingly larger fiber is probably to be sought in the need for adequate surface for transference of food and gases. The number of units is regulated by a functional need, so that all necessary permutations and combinations of afferent stimuli can be adequately translated into motor responses.

6. The information presented in this section is taken from two sources: (*a*) Borcroft, J.: Features in the Architecture of Physiological Function, London, Cambridge University Press, 1934. (*b*) Holmes, G.: The Cerebral Integration of the Ocular Movements, Brit. M. J. **2**:107, 1938.

The brain stem contains a complex mechanism by which the ocular movements are effected and coordinated. These movements are of three kinds:

1. Movements which occur in response to volition.

2. Movements which occur involuntarily as a response to such stimuli as a peripheral flash of light, a sound or the necessity to bring about movements of the eyes to make possible fusion of the images of the two retinas.

3. Movements of compensation and adjustment, which occur when the gaze is kept fixed on an object of interest while the head or the object moves.

The brain stem mechanism is subordinated to impulses which are cortical in origin. All movements of the muscles, those of the eyes as well as those of the arms and legs, are directly or indirectly initiated or controlled by afferent impulses. For the eyes the most important afferent impulses originate in the retina and the labyrinth, acting either alone or in conjunction with proprioceptive impulses from the muscles of the neck. These impulses insure correct postural adjustments of the eyes to changes of the position of the head in space.

There are two cortical areas of great importance, a frontal and an occipital area. The frontal area is separated from the precentral motor gyrus by inexcitable cortex. The projection fibers from this frontal center pass through the anterior part of the internal capsule and then probably enter the cerebral peduncle and turn dorsalward into the tegmentum.

The occipital area is probably not the area striatum but the surrounding contiguous tissue. Electrical stimulation of the inner aspect of the occipital lobes brings about ocular movements, and that these movements are not due merely to subjective visual impressions which activate the frontal lobes is shown by the fact that they cannot be evoked when the occipital lobe has been completely isolated from the rest of the cortex. Fibers from this area descend medially to the optic radiations and from there through the pulvinar and the anterior brachium to the tectum of the midbrain.

When the function of the frontal center is disturbed, the most striking feature is inability to move the eyes on command, although they can follow a very slowly moving object or a row of dots.

The ability to follow print or a row of dots despite paralysis of the frontal center depends on a strong reflex—the fixation reflex, for which integrity of the occipital cortex is necessary.

Fixation means the maintenance of postures by the eyes by tonic contraction of the ocular muscles so that the retinal images fall on the fovea. The eyeballs, however, are not held immobile but rather oscillate

constantly through a small arc, so that sensory adaptation will not bring about disturbing after-images. The slightest movement of the head makes necessary a compensatory movement of the eyes in the orbit. Normally fixation is under control of the will, but when the frontal center is defective the fixation reflex may be so strong that the eyes can be moved only when the reflex is broken by interruption of the retinal impulse. Even in adult life a flash of light on the periphery of the retina attracts one's gaze involuntarily and reflexly, but in addition to consciousness the reflex requires interest and attention.

Fixation is most readily held when the eyes are near their position of rest. Then involuntary effort alone may suffice. When the eyes are turned far from the midline, however, fixation requires much energy and the eyes tire readily even when a normal fixation reflex is active.

The integrity of the occipital cortical area is necessary for several other functions. Fusional movements and accommodations depend on it. The involuntary movements of the eyes toward a point whose image has fallen extrafoveally are mediated through the occipital cortex, as is also the reflex for the maintenance of fixation of a stationary or a moving point.

DISCUSSION OF MOOT POINTS

Many questions arise concerning the significance of the individual components and manifestations of the clinical complex known as divergence excess as well as concerning the complex as a whole. All of these questions cannot be answered by available data. Some cannot be answered at all. For some the several data are conflicting. For others the best that can be done is to state them clearly, freed from unjustified assumptions. In the paragraphs that follow an attempt is made to present the data which pertain to each topic and to discuss the significance of the concepts which are current.

Since the evidence does not represent an unbroken, logical series of thought, it will be presented as disconnected fragments. These fragments will be grouped as they throw light on the more important questions.

Definition.—The simplest definition seems to be that of Bruce:[7] "If a patient has excessive divergence, he has divergence excess." One is impelled to ask "in excess of what?" Clearly, actual divergence of the visual axes cannot be meant, for divergence excess is not used in the same sense as exotropia. The definition is not informative until one defines divergence. A descriptive definition is probably more appropriate in the present state of knowledge—one that merely lists the characteristics of the clinical entity. The definitions of Duane, Dunnington and Berens and his associates are such descriptions.

7. Bruce, G. M.: Ocular Divergence: Its Physiology and Pathology, Arch. Ophth. **13**:639 (April) 1935.

Divergence.—One must distinguish the act of diverging from divergence conceived of as a well established functional unit of the binocular neuromuscular system for whose performance an anatomic structure exists in the brain. It is, however, not necessary to assume that such a functional unit exists. The visual axes do indeed diverge and converge frequently in the course of binocular adjustment, but they may do so as a result of an orderly sequence of impulses to the individual muscles, just as the fingers are moved with equal accuracy, precision and speed in such complex acts as are necessary in using a typewriter or a musical instrument. The evidence for the belief that divergence exists as an independent anatomic functional unit is summarized by Bruce.[7] The most important evidence for the existence of a divergence center is the fact that divergence can be paralyzed. To support this there is abundant clinical evidence. Bruce summarized the speculative evidence for existence of a center for divergence separate from, but adjacent to, the nucleus of the sixth nerve. Since the external rectus muscles are innervated only ipsilaterally, this nucleus would probably be in the midline.

Bender and Savitsky [8] have reported clinical descriptions and studies of histologic preparations in the case of a patient who had paralysis of divergence and in whom the only lesion demonstrable at autopsy was a cavernous hemangioma in the central gray matter surrounding the aqueduct of Sylvius, near the oculomotor nuclei.

One must remember, however, that such destruction of a function is not incontrovertible proof of the existence of a divergence center. At least, it is not evidence that divergence is an independently organized unit in a person's mechanism for purposive control and adjustment of binocular movements for which an anatomic unit of brain called a center is provided. If divergence were less a primordial unit but rather a movement that had been learned because it had proved useful, it would still be performed as a result of impulses which would habitually be carried by the same neurons, as is a conditioned reflex. If these particular neurons were destroyed, the function would also be destroyed.

Bielschowsky [5] expressed the opinion that divergence innervation is necessary not only to change the convergence of the visual lines into parallelism but to overcome esophoria. Also, it is hardly conceivable that of all the innervations of the ocular muscles the convergence innervation alone should lack an antagonistic innervation. Faith in the existence of divergence as an independent function is increased by habitually thinking of convergence and divergence in terms of an oversimplified scheme of opposing forces acting only in a horizontal plane. When a more com-

8. Bender, M. B., and Savitsky, N.: Paralysis of Divergence, Arch. Ophth. **23**:1046 (May) 1940.

plex movement is considered, such as carrying the eyes up and out, the accomplishment of a final precise adjustment by means of the same simple stimulus to diverge as is active in a horizontal plane is harder to imagine, because the twelve extraocular muscles must be stimulated and inhibited in entirely different proportions.

The amount of prism which can be overcome in the interest of binocular single vision is often referred to as divergence power. The use of this word is to be deprecated, because it is inaccurate, and its consistent use induces one to think unconsciously of divergence as a power. Power is defined by the physicist as the ability to do work in a unit of time. There is no time element in divergence. An eye that can overcome 6 prism diopters of prism base in can do so, if not indefinitely, at least for a very long period, and it is not possible to find increasingly longer periods for smaller prisms and shorter periods for greater prisms, as would be the case with a function that really is a power. It is not even known that anything resists the functional agency that brings about divergence. Whether energy is expended in a reciprocal antagonism between centers of convergence and divergence is not known. One still sees, however, many statements in the ophthalmologic literature that suggest that convergence and divergence are thought of as entities which resist one another. For instance, Duane postulated that divergence excess may be secondary to convergence insufficiency, which suggests that he had in mind that inadequate resistance on the part of the convergence mechanism allows the divergence mechanism to function unduly.

As a matter of fact, although such measurements as the gram-centimeters of pull of the individual ocular muscles are no longer stressed, one often thinks of ocular muscles in physical rather than in biologic terms. Colson [9] distinguished between conventional and real abduction. Real abduction was used by him as the term for the prism divergence to which has been added the amount of esophoria or from which has been subtracted the amount of exophoria. Such an operation with symbols applies acceptance of a definite quantitative relation between heterophoria and divergence. From the statements one cannot conclude that the author considered divergence a factor in the production of the heterophoria. He must have believed, however, that the numerical value of the heterophoria represents a position of the eyeballs from which the divergence factor begins to pull. Exophoria, for example, seems to be an advantage to the postulated force or power of divergence, in that it has to function less to bring about a given amount of divergence.

That divergence is actually a factor in bringing about a given heterophoria is an assumption implied in the writings of many oculists.

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9. Colson, Z. W.: The Effect of Alcohol on Vision, J. A. M. A. **115**:1525 (Nov. 2) 1940.

To cite an example, Prangen and Koch [10] stated that "divergence insufficiency is distinguished from other types of esophoria."

A systematic investigation of the relation of convergence and divergence has been reported by me.[11] In 1,000 consecutive clinical records it was found that the values for convergence and divergence in no way determined the lateral heterophoria. The patients were grouped according to the magnitude of divergence. In each group a full range of convergences was found, and the heterophoria associated with it was not in any way related quantitatively to it. One may conclude from this either (1) that convergence and divergence as unit integrated functions are not concerned in the production of heterophoria or (2) that the tests for divergence and convergence are not adequate methods of estimating these functions. The latter conclusion may well be true. It is known that pairs of eyes differ in the angle of divergence which they can achieve in order to maintain binocular single vision. It is not known in detail what is the nature of the mechanism that brings this about, nor is anything known about its expenditure of energy. It is quite possible that one is not measuring a pull against resistance but an end position of a movement which is limited by the mechanism provided for its turning. A prism divergence of 8 D. may not indicate that the pair of eyes tested is working twice as hard as a pair capable of a prism divergence of 4 D., nor is the contrary necessarily true, that a pair of eyes whose maximum effort can bring about only 4 D. of divergence is working against twice as great a resistance. It is equally possible that the number of neurons habituated to the task is greater in one person than another and that although he has a greater possible range of divergence, it is no more and no less tiresome to use this mechanism. It might be useful to view the coordination of ocular movements as a problem in traffic management rather than a tug of war. The tests may give some information as to the efficiency with which the organism handles this problem, but possibly only a gross approximation.

Possibly variation of divergence within a normal range is of no significance. One must not forget, however, that there are patients who can overcome 30 degrees of diverging prism, and, although they are able to maintain binocular single vision intermittently or even continuously for a long time, they must eventually so adjust their oculomotor system that exotropia results.

Writers also refer to divergence excess which is secondary to convergence insufficiency and vice versa. I have found no publication of the record of an individual patient in whom such reciprocal changes in

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10. Prangen, A. de H., and Koch, F. P.: Divergence Insufficiency: A Clinical Study, Tr. Am. Ophth. Soc. **35**:136, 1937.

11. Haessler, F. H.: Relationship of Heterophoria to Divergence and Convergence, Based on Clinical Measurements, Tr. Am. Ophth. Soc. **35**:149, 1937.

the magnitude of convergence and divergence have been measured from time to time in the course of years.

Heterophoria.—The phenomenon classed as heterophoria is variously interpreted as a measure of the position of rest of the eyeballs, the position assumed when the muscles are relaxed, and also as an indication of a state of equilibrium between such forces as divergence and convergence. It is sometimes referred to as latent squint or as a tendency of the eyes to deviate during binocular fixation. Verhoeff [12] pointed out that the tests measure not a condition or a tendency that exists during fixation but an actual deviation which occurs during absence of fixation. It is a mere assumption that the deviation is a measure of the heterophoria.

The importance of the part played by the fusion impulse must not be underestimated. Fischer [13] concluded that it is by far the most important mechanism which makes possible the precise collaboration of the two halves of the paired organ of vision. If the magnitude of heterophoria is a measure of the factors concerned in binocular coordination, exclusive of the fusion impulse, three or more factors may exist, one or more of which are assumed as given in discussions of heterophoria. These factors are:

1. The lasting tonic contraction existing in the plastic tonus of muscles maintaining posture.

2. The various mechanical and anatomic factors, such as the size and shape of the orbits, the position of the orbits in relation to one another, the size and shape of the eyeball, the position of the eyeball in the orbit, the length and resistance of the extraocular muscles and the physiologic properties of the other orbital contents and of the eyelids.

3. A possible balance that may exist between a convergence impulse and one of divergence, the resultant effect of which is the proper reciprocal innervation of a group of extraocular muscles to bring about purposive binocular adjustment.

In support of the second of these factors one may cite Bielschowsky's [4] statement that he considered it the predominant determinant factor of the adjustments which determine heterophoria.

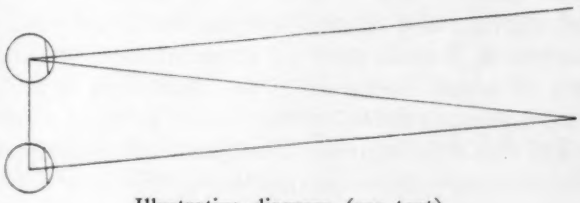
The third factor is implicitly accepted by Duane and his followers when they diagnose, for example, esophoria due to divergence insufficiency or exophoria due to divergence excess.

In many reports authors mention the importance of measuring heterophoria for near as well as for distant vision. A point that seems to have escaped notice is this: If a measurement for near vision is to have

12. Verhoeff, F. H.: Hyperphoria Tests Based on a New Principle, Arch. Ophth. **22**:743 (Nov.) 1939.

13. Fischer, M. H.: Beiträge und kritische Studien zur Heterophoriafrage auf Grund systematischer Untersuchungen, Arch. f. Ophth. **108**:251, 1922.

any significant interpretation it must be made not at any distance near at hand but at a known, precisely measured distance. A glance at the accompanying illustration will make clear the importance of this. If two eyes whose axes are parallel and over one of which a Maddox rod is placed view a distant light, the red line will seem to be on the light, and the result of the test will be recorded as orthophoria. If no change in these conditions is made except that the distance from the eyes to the light that is to be viewed is changed to 30 cm., the line will seem to be to the left of the light, and exophoria will be recorded. The magnitude of this exophoria is determined not only by the distance between the light and the base line passing through the centers of rotation of the eyeballs but by the interpupillary distance. The angle of correction of this reading is equal to the angle of convergence for a pair of eyes of known interpupillary distance converging on a point at which laterophoria for near vision is measured. If this distance is 30 cm., the angle of correc-



Illustrative diagram (see text).

tion (to the nearest 0.5 degree) for each 2 mm. of interpupillary distance is as follows:

Pupillary distance, mm....	50	52	54	56	58	60	62	64	66	68	70	72	74	76
Angle of convergence at 30 cm., degrees.....	9.5	10	10.5	11	11	11.5	12	12.5	13	13	13.5	14	14.5	15

If factor 2 is considered the predominant one, then a correction must be made in the Maddox rod tests for near vision if the notation is to represent the significant position of the optic axes, that is, the deviation from parallelism. The tabulation lists the corrections that must be made.

If, on the other hand, factor 3 is considered the predominant one, then in all probability the information one seeks in measuring with the Maddox rod for near vision is the deviation of the axes from the convergent position which would give binocular single vision at this distance. The direct reading of the Maddox rod would give this information, but it will be precise only if the distance between the base line connecting the center of rotation and the light has been precisely measured.

Clark's [14] study of the movements of the eyes during reading suggests that any association that may exist between laterophoria and divergence

14. Clark, B.: A Case of High Esophoria Studied by Eye Movement Photography, Am. J. Ophth. **19**:503, 1936.

is not definitely and precisely fixed. He found that normal eyes definitely overconverge during the interfixation movement and that an abductive adjustment becomes necessary during the first part of fixation. In 1 subject, with very high esophoria, the overconvergence was no greater than in the normal group.

Convergence and Accommodation.—Convergence need not be discussed in detail, because it is a function similar in nature to divergence. I shall merely point out that convergence and accommodation are associated in the normal process of vision. There is a limited range in which they can be dissociated, usually spoken of as relative convergence. For this reason the state of accommodation may on occasion be used as an index of the activity of convergence. In his analysis of the case of divergence excess reported by Bielschowsky,[15] he concluded that because the ciliary muscle was maximally contracted, the associated convergence impulse was also in a state approaching maximal activity and that it was necessary for it to assume this function to counteract a hyperkinetic functioning of divergence.

The Clinical Entity as a Whole.—Consideration of the clinical entity divergence excess as a whole does not throw much light on the details of the process by which divergence of the visual axes is accomplished. Empiric observation has established that such a group of symptoms and signs exists and that it is frequently associated with asthenopia. There is also general agreement that severe grades may lead to actual exotropia. It is, however, not possible to say which manifestations are essential and which are accidental. In particular, there is no proof that measurements for near vision must be normal in order to rule out a complicating disorder convergence. Since the mechanism and significance of each of the units which make up the whole clinical entity are imperfectly understood, it is clearly impossible to make unequivocal assertions about their relative importance. Even a therapeutic test is not available. Much of the therapy is applied on rather general indications or on the basis of assumptions which are valid only with varying degrees of probability. Sometimes therapeutic measures restore the patient to comfort without changing the objective manifestations.

It is sometimes objected that success in treating divergence excess is erroneously ascribed to a cure of this condition when the real cause of discomfort in those cases of muscular imbalance is a convergence insufficiency. Some authors assert that in cases of pure divergence excess the measurement of muscle balance for near vision must be normal. They believe that divergence functions only for distant gaze. This is, however, not consistent with generally held assumptions. If divergence is an innervation that functions as antagonist to convergence, it must be active at all distances.

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15. Bielschowsky (footnotes 4 and 5).

After reviewing all the pertinent data, one must conclude that it is essential to realize that the entire matter is a biologic problem. In biology the emphasis is necessarily on empiric observation, and explanatory patterns are adopted cautiously and tentatively, with full realization that they must be constantly revised as fresh evidence is collected. The geometric explanations and constructions must be accepted with great caution. They are based on the assumption that the afferent impulses which ultimately control the motor adjustments depend on the appreciation by the sensory mechanisms of angular quantities. It is equally possible, however, that only direction and distance of the image of the second eye in relation to that of the guiding eye are perceived and that adjustments are made by constant sensory checking of the results as motor adjustments are made.

Therapy.—Three methods of treatment are used for patients presenting the symptoms of divergence excess, namely, prisms for wear, surgical intervention and orthoptic training.

Neither prisms nor operative treatment can influence a hyperkinetic divergence function; hence these need not be included in this discussion. They are indicated on the basis of experience and assumptions which hold for muscular imbalances in general, usually under the diagnosis of heterophoria or heterotropia. Prisms do not find favor with many and seem to be only of temporary benefit. Surgical procedures are of inestimable benefit to many patients. A discussion of them is omitted, not because I believe them inadequate to influencing the empiric disease complex but because they cannot have any effect on a hyperkinetic divergence impulse.

If that can be influenced, it is by orthoptic training. It must be emphasized that orthoptic procedures, although often called exercises, are not effective in the way that calisthenic exercises are. Their purpose is not to strengthen muscles. They are a form of reeducation of the neuromuscular system. Orthoptic treatment may in any case of divergence excess be effective in one or more of three ways:

It may increase the patient's awareness of the image from each eye.

It may stimulate the patient's appreciation of the proprioceptive impulses from the extraocular muscles.

It may increase the permeability of the paths from the cortical centers and so stimulate the fixation reflex.

By increasing the factors of nervous control it may bring about more harmonious function of the several parts of the system.

SUMMARY

Divergence excess is a clinical entity characterized by exophoria which is greater for distance than for near vision, excessive divergence and usually normal convergence. With the severe grades there fre-

quently develops exotropia, which at first is intermittent but finally becomes constant. Whether the condition of the 1 to 2 per cent of patients who have similar manifestations but do not have exotropia is caused by the same factors in less degree has not been demonstrated.

The clinical diagnosis and the explanation of the process of development of divergence excess are based on interpretations of measurements of exophoria and prism divergence.

Exophoria is interpreted as latent divergence and as a deviation from the position of rest. Tests for exophoria actually give information only as to the position which the optic axes assume when stimuli for binocular fusion have been avoided as much as possible. The relative absence of precision of this last objective statement indicates the inadequate understanding of the mechanism of the neuromuscular adjustments in question. Although exophoria is widely assumed to be a result of the opposing "forces," divergence and convergence, this has not been conclusively demonstrated. At least two factors are of great importance: (*a*) the anatomic and mechanical factor and (*b*) the tonic impulses responsible for postural adjustment, which may or may not be organized into more highly integrated functional units, such as divergence.

The divergence of the optic axes stimulated by abducting prisms is assumed to be a measure of a divergence impulse. The often immeasurable factors, *a* and *b*, under exophoria would greatly modify this value.

An essentially different view has been expressed by Bielschowsky. In the case of the only patient with divergence excess whom he has seen, he deduced an excessive divergence impulse from excessive activity of convergence function which was indicated by spasm of the associated function of accommodation.

The known facts of neuromuscular physiology do not give support to some widely accepted assumptions. Great caution against an oversimplified, almost geometric, interpretation is indicated.

The fact to emphasize is that movements of the extraocular muscles are initiated and controlled by afferent visual and proprioceptive impulses. Probably no purposeful movement is executed without participation of one of two cortical areas. There are a frontal cortical area that takes part in voluntary ocular movements and an occipital area the integrity of which is necessry for the fixation reflex, fusional movements and accommodation.

It is under the control of these cortical centers that the motor nuclei and centers in the brain stem bring about integrated ocular movements.

There is presumptive evidence that there are in the brain stem centers for such integrative unit functions as divergence and convergence. Whether these exist as preformed anatomic masses intended in the pattern of embryonic development for the specific function or whether undifferentiated paths are habitually associated with the frequently repeated act of diverging is perhaps an academic question.

News and Notes

PERSONAL

Dr. Arthur J. Bedell.—Dr. Arthur J. Bedell, clinical professor emeritus in ophthalmology and otolaryngology at Albany Medical College, received the honorary degree of Doctor of Science at Hobart College, Geneva, N. Y., at commencement, May 26. He also received the honorary degree of Doctor of Science at the University of Colorado, Boulder, Colo., at commencement, June 9.

Habana University.—Dr. C. E. Finlay has been appointed emeritus professor of ophthalmology. Dr. J. M. Penichet, a graduate of Georgetown University School of Medicine and previously an assistant professor, has been appointed to the chair of ophthalmology.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Bacteriology and Serology

PROPHYLACTIC AND THERAPEUTIC EFFECT OF BACTERIOPHAGE AND OF ANTIVIRUS IN EXPERIMENTAL STAPHYLOCOCCUS INFECTION OF THE EYE. J. BRONFENBRENNER and S. E. SULKIN, Am. J. Ophth. **22:** 1321 (Dec.) 1939.

Bronfenbrenner and Sulkin describe their method of producing lesions, the appearance of the lesions and their experiments. They reach the following conclusions.

"1. Instillations of antivirus or bacteriophage into the conjunctival sac are not sufficient to protect the cornea or the anterior chamber of the eye against a severe infection.

"2. Direct application of antivirus or bacteriophage is of no value in the treatment of eyes experimentally infected with staphylococci.

"3. Furthermore, intensification of the local reaction frequently results from the application of bacteriophage or antivirus to the lesion."

W. S. REESE.

Biochemistry

ASTHENOPIA DUE TO VITAMIN-A DEFICIENCY. F. C. CORDES and D. O. HARRINGTON, Am. J. Ophth. **22:** 1343 (Dec.) 1939.

Cordes and Harrington give the following summary of their clinical survey of cases of asthenopia apparently due to vitamin A deficiency.

"This report presents a review of 82 cases of persistent asthenopia in which it is felt vitamin-A deficiency, as judged by the Bio-Photometer, was the causative factor. The Bio-Photometer readings varied between 0.7 and 4.2 mft-c, the average being 2.09. In this group a history of night blindness was obtainable in only 22 percent of the cases. In 30.5 percent there was an apparent deficiency in diet, while 17 percent of the patients gave a history of chronic gastrointestinal disease, usually chronic colitis.

"These patients were treated with carotene in oil, the average dose being 30,000 units daily. Of the patients on this therapy 79 percent obtained complete and 12 per cent partial relief from their symptoms. In the majority of patients it was necessary to continue small doses of carotene to maintain a balance. Forty percent of the cases were observed for a period of over six months and 20 percent between one and two years.

"The symptoms that persisted after the usual causes of asthenopia had been corrected were consistent enough to suggest the following symptom complex as being typical of vitamin-A deficiency:

"The patients complained of photophobia associated with pain and rapid fatigue of the eyes upon use, especially at night; difficulty in

reading for longer than 15 to 20 minutes, with the print at times blurring momentarily. Driving and the movies caused headache and blurring in a fairly high percentage. A chronic persistent conjunctivitis was a rather frequent finding. Often these symptoms were associated with a deficiency in diet or gastrointestinal disease, especially chronic colitis.

"In the series reported here, carotene in oil was the source of vitamin A. From the literature, however, it appears that there is little difference whether vitamin A units are taken as cod-liver oil, Vitamin-A concentrates, or carotene.

"If, as noted above, any disturbance is present which increases the metabolic need for vitamin A or hinders its absorption or storage, larger than normal amounts of vitamin A are necessary. This explains the reason for the necessity of continued use of carotene in some instances even though the diet was corrected.

"It is hoped that this preliminary report may stimulate others to further study the clinical effect of vitamin-A deficiency on the normal functions of the eye."

W. S. REESE.

Conjunctiva

A CASE OF RHINOSPORIDIUM OF THE CONJUNCTIVA. W. B. ANDERSON and T. H. BYRNES, Am. J. Ophth. **22:** 1383 (Dec.) 1939.

A 12 year old Negro complained of a slowly growing tumor on his left eye, present for one year. At the time of examination it was interfering with closure of the lid. Examination revealed an irregularly lobulated, pinkish red growth protruding from beneath the lower lid, near the external canthus. It was pedunculated and was attached in the fornix by a broad base. It resembled the fungoid granulation seen following curettement of a chalazion. It was removed and sent to the laboratory, where a diagnosis of conjunctival rhinosporidiosis was made.

W. S. REESE.

RHINOSPORIDIOSIS. E. W. GRIFFEY, Am. J. Ophth. **22:** 1389 (Dec.) 1939.

Griffey reports the case of a 10 year old white boy with a small strawberry-colored mass on his right caruncle. The boy lived on a farm and helped to care for horses and cows. The mass was solid, nodular and encapsulated and was attached to the upper edge of the caruncle by a thin stalk. It was 12 by 10 by 16 mm., and it prevented the lids from closing. It was excised and sent to the Army Medical Museum, where a diagnosis of rhinosporidosis of the scleral conjunctiva was made.

W. S. REESE.

ERYTHEMA NODOSUM WITH INVOLVEMENT OF THE CONJUNCTIVA. E. KISSIN, Vestnik oftal. **16:** 506, 1940.

Kissin found only 6 previously reported cases of erythema nodosum of the skin in which the conjunctiva was affected. In all cases bilateral involvement of the conjunctiva was observed. A woman aged 50

complained of general malaise and "blisters" of the skin of both legs and one shoulder of one week's duration; prior to this she had had a sore throat for four days. There were a number of firm, painful nodules on the legs and on the left shoulder. There was a solitary nodule on the temporal side of the conjunctiva of each eye, about 3 mm. from the limbus, at the palpebral fissure. Its diameter was 5 or 6 mm.; it was heavily vascularized, with distinct borders. Bacteriologic examination showed hemolytic streptococci in the throat and conjunctiva and also a great number of leukocytes (pyelitis) in the urine. The ocular and the general symptoms disappeared coincidentally with absorption of the cutaneous lesions.

This benign course of erythema nodosum, despite the severe clinical symptoms, suggests that the disease is allergic. In the case reported, local allergy of the conjunctiva in relation to the hemolytic streptococcus is suggested.

O. SITCHEVSKA.

Cornea and Sclera

CLINICAL AND ANATOMIC RESEARCH ON A HITHERTO UNKNOWN DOMINANTLY INHERITED DYSTROPHY OF THE CORNEAL EPITHELIUM. A. MEESMANN and F. WILKE, Klin. Monatsbl. f. Augenh. **103:** 361 (Oct.-Nov.) 1939.

The authors render a detailed report on dystrophy of the corneal epithelium in three families, the genealogic trees of two of which are given. The divers manifestations in several generations of these families are described in detail and are well illustrated by seventeen pictures, some of them colored, showing the appearance with the slit lamp and the microscope.

This type of dystrophy of the corneal epithelium, hitherto unknown, is well defined. Its differentiation from the three accepted types and from several special types of hereditary dystrophy of the cornea is discussed. Some of the essential features are dotted and vesicular opacities in the corneal epithelium, observed with the slit lamp, with slight roughness of the corneal surface and pain recurring in attacks. The disease begins in early childhood and progresses at intervals up to advanced age. The visual disturbances are moderate, hardly ever leading to invalidism. The authors report that the deeper strata of the cornea were involved in only 3 patients, who presented linear, curved or striated opacities in or about Bowman's membrane. The corneal nerves were not disturbed. Simple dominant heredity was evident in 34 persons of the two genealogic trees. Histologic examination showed epithelial dystrophy, with its typical epithelial changes, and glycogen stored in the cells. Some of the patients had secondary corneal opacities, caused by eczema; they presented unusually early yellowish discoloration of the scars, described previously in another connection. Hyaline globules were found in the corneal propria only in some instances; differential staining proved them to be related to elaidin. The epithelial dystrophy was especially well developed beneath the yellowish scars.

K. L. STOLL.

PRIMARY RIBBON-SHAPED DEGENERATION OF THE CORNEA: REPORT OF A CASE. R. KLAINGUTI, Klin. Monatsbl. f. Augenh. **103:** 478 (Oct.-Nov.) 1939.

The eyes of a man aged 53 were observed by the author for fifteen years. A ribbon-shaped greenish opacity about 4 to 5 mm. in width was noted in the cornea. It terminated as a serrated line near the temporal and nasal limbus and was separated from the gerontoxon by a fine translucent line. A net-shaped opacity was present in the center of the cornea. The opacity was located in Bowman's membrane. The opacity was less advanced in the left eye. Both eyes were free from other changes. No members of the patient's family were afflicted with a similar ocular disease. No cause could be found. Eyes with similar corneal opacities were examined histologically by other authors. They showed hyaline degeneration and lime deposits in Bowman's membrane, suggesting local trophic disturbances.

K. L. STOLL.

POSTOPERATIVE COURSE IN CASES OF KERATOPLASTY. I. A. WASSERMAN, Vestnik oftal. **16:** 410, 1940.

The results of the postoperative course and care of 300 patients treated by partial penetrating corneal transplantation are reported.

The conjunctival flap was removed in four to five days after the operation (in the cases of children and in complicated cases, in seven to fourteen days). An elevation of the transplant was noticed in the majority of the cases after removal of the flap.

The difference in the level was due either to the transplant being thicker or to the imperfect technic of the operation, i. e., to the fact that the transplant was not in the same horizontal plane as the leukoma. The postoperative course was not affected by the elevation of the transplant. In some cases small slits formed in the transplant at the periphery, probably because of stretching.

The reforming of the anterior chamber usually took place on the fourth or fifth day; a delay was noticed in cases of interstitial keratitis, as in such cases the anterior chamber was restored in eight to ten days after the operation.

The transplant frequently became opaque after the operation. Filatov's school (contrary to Elshnig's school) believes that this occurs either because of the inflammatory process (iridocyclitis) or because of the increase of intraocular tension. Measures for combating glaucoma and iritis lead to clearing of the opacities in the transplant.

Osmotherapy, autohemotherapy, transplantation of conserved skin and subconjunctival implantation of placenta are of some value in clearing the opaque transplant. The transplant is frequently opaque in cases of interstitial keratitis (40 per cent), as a serofibrinous exudate forms which causes anterior synechia followed by secondary glaucoma.

The most serious complication is glaucoma. For patients in whom glaucoma is present prior to keratoplasty no conservative or operative measures are of any great value, as the transplant usually does not clear up once it has become opaque. In another group of patients glaucoma was the result of anterior synechia; miotics were used frequently preoperatively, and antiglaucomatous operations were performed in four to

six weeks after keratoplasty. In a third group of cases glaucoma was the direct complication of the transplantation, and most of the patients suffered from interstitial keratitis; antiglaucomatous operations were usually successful.

Vascularization was observed in many patients on the sixth to the tenth day (at latest two months after the operation), and it ran parallel to the development of an inflammatory course. Blood vessels occasionally appeared without the transplant becoming opaque.

A change in refraction was noted one or two months after transplantation; myopia at first would shift to hypermetropia. This was probably due to the formation and organizing of the ring around the transplant.

These various complications are discussed and illustrated with case reports.

O. SITCHEVSKA.

Experimental Pathology

PRELIMINARY ANALYSIS OF FUNCTIONS OF THE TEMPORAL LOBES IN MONKEYS. H. KLUVER and P. C. BUCY, Arch. Neurol. & Psychiat. **42**: 979 (Dec.) 1939.

The authors report a continuation of work reported in the *American Journal of Physiology* in 1939 and in the *Journal of Psychology* in 1938.

The effects on behavior of the removal of both temporal lobes, including the uncus and the greater part of the hippocampus, were studied in macaques. The monkeys exhibited the following symptoms: (1) forms of behavior which seem to be indicative of "psychic blindness"; (2) strong oral tendencies in examining available objects (licking, biting gently, chewing, touching with the lips, "smelling"); (3) a strong tendency to attend and react to every visual stimulus ("hypermetamorphosis"); (4) marked changes in emotional behavior or absence of emotional reactions in the sense that the motor and vocal reactions generally associated with anger and fear were not exhibited, and (5) an increase in sexual activity. These symptoms also appeared if the olfactory tracts were cut previous to removal of both temporal lobes. Even the oral tendencies, except for the "smelling," were present.

The symptoms typical of monkeys with both temporal lobes removed did not appear after (1) bilateral removal of the first temporal convolution; (2) bilateral removal of the second and third temporal convolutions; (3) severing of the connections between the temporal and the frontal lobe, i. e., duplication of the anterosuperior margin of the lesion produced by temporal lobectomy or (4) severing the connections between the temporal and the occipital lobe, i. e., duplication of the posterior margin of the lesion produced by temporal lobectomy. The symptoms did not appear, moreover, after unilateral temporal lobectomy, except that there was in some cases a change in the direction of greater "tameness." This "tameness" was also observed when after previous extirpation of both prefrontal areas one temporal lobe was removed.

Differential reactions to visual stimuli established preoperatively were seriously disturbed after bilateral temporal lobectomy, but it was possible to reestablish the response through training. The ability to "generalize" in responding to visual stimuli did not seem to be impaired.

R. IRVINE.

Injuries

TETANUS AND THE PROPHYLACTIC USE OF ANTITOXIN FOLLOWING INJURIES OF THE EYE. D. G. COGAN, Am. J. Ophth. **22:** 1365 (Dec.) 1939.

After a discussion of the use of tetanus antitoxin Cogan draws the following conclusions.

"The development of tetanus following ocular injury is usually, if not always, associated with panophthalmitis. This panophthalmitis, however, is caused by organisms other than B. tetani. Enucleation does not offer any assurance against the development of generalized tetanus even when performed during the first 24 hours after the injury, and apparently does not affect the mortality rate.

"Tetanus following ocular injury is obviously a rare catastrophe, for it has been reported in the literature only 20 times. That this relative infrequency is not simply the result of prophylactic antitoxin is apparent from the fact that there were only 14 case reports of the condition in the entire world literature before the days of prophylactic antitoxin. In view of this relative infrequency and of the danger incident to the administration of serum, it might seem that prophylactic use of antitoxin is never indicated following ocular injury. But practically all those injuries that did result in tetanus had been caused by objects associated with horses directly or with ground probably contaminated by manure. It would seem justifiable, therefore, to give antitoxin in those cases in which there is a history of such contamination. These would actually comprise a very small percentage of the total number of cases of injury to the eye. While a single prophylactic injection of 1,500 units is probably adequate, repetition of this once during the first week would be justified as an added precaution."

W. S. REESE.

Instruments

A BODKIN FOR STRABISMUS OPERATIONS. W. O. LODGE, Brit. J. Ophth. **24:** 407 (Aug.) 1940.

This is a modification of a miniature self-retaining strabismus hook which the author had previously devised. The bodkin is made of thicker stainless steel wire. The handle and the hook with its terminal eye are ground to the original gage. The middle third is forged into a grooved director, curved on the flat. The bodkin renders an extraocular muscle accessible and puts it to rest. The dimensions of the instrument are given in detail.

The article is illustrated.

W. ZENTMAYER.

A NEW KNIFE FOR DOING VAN-MILLINGEN'S GRAFTING OPERATION. SABRI KAMEL, Brit. J. Ophth. **24:** 567 (Nov.) 1940.

It may be recalled that Van-Millingen's operation was devised for trichiasis, usually of trachomatous origin. It consists in the formation of a groove in the intermarginal space of the lid, posterior to the eyelashes, partially splitting the tarsus, in which a mucous graft from the lip is inlaid. The handle of the instrument is 9.5 cm. long and is of solid metal.

The blade is approximately 1.5 cm. long. The base is about 4 mm. in breadth. The sides of the blade, beginning from the base, are slightly curved, with both convexities toward the outside, and they meet in a pointed, sharp end. The blade is sharp on both sides. It is slightly thick in the center, becoming thin as it passes toward both sides and toward the tip. The blades make an angle of 120 degrees with the handle.

The article is illustrated.

W. ZENTMAYER.

Lens

PROPHYLACTIC FOREIGN-PROTEIN THERAPY IN CATARACT EXTRACTION. C. A. NOE, Am. J. Ophth. **22:** 1014 (Sept.) 1939.

After study of 150 patients, Noe draws the following conclusions:

"1. Prophylactic intravenous administration of typhoid-H antigen (Lilly) apparently lessens the inflammatory reaction after cataract extraction, and gives rise to both 'O' and 'H' antibodies in the blood.

"2. There seems to be no definite relationship between blood antibody titer and postoperative reaction.

"3. Omnadin (Winthrop) produced no change in postoperative reaction from the control series. [According to the manufacturer, omnadin is a compound sterile solution of protein (obtained from nonpathogenic bacteria), various animal fats, and lipoids derived from bile.]

"4. Typhoid-H antigen (Lilly) must be used with great caution in old people with pathologic vascular systems."

W. S. REESE.

TREATMENT OF INCIPIENT CATARACT WITH ASCORBIC ACID. V. MUHLMANN, B. V. RE and R. LACHMAN, Arch. de oftal. de Buenos Aires **14:** 552 (July) 1939.

After an extensive review of the literature on the treatment of incipient cataract with ascorbic acid, the authors report their experience in 60 cases. There was no special selection of cases from a general or a local viewpoint. Determination of the urinary level of ascorbic acid was used as a test but was later given up in favor of Portnoy's intradermal reaction for hypovitaminosis C based on the rapidity of absorption of 2,6-dichlorophenolindophenol. In the early cases the ascorbic acid was administered by intramuscular and intravenous injection; in the later cases, intravenously only. The results obtained were improvement in 51.22 per cent of cases; retardation of the progress of the cataract in 38.95 per cent, and continued development of the cataract in 9.73 per cent.

They conclude that there are no contraindications to this method of treatment; that it is of use only for incipient cataract with vision of 0.5 or better, and that the treatment must be kept up for a long time.

C. E. FINLAY.

THE AUREOLE, A PHYSIOLOGIC PHENOMENON IN THE ANTERIOR SURFACE OF THE LENS: REPORT OF CASES. M. BÜCKLERS, Klin. Monatsbl. f. Augenh. **103:** 413 (Oct.-Nov.) 1939.

In his research on the connection between neurodermatitis and cataract, Bücklers observed extremely fine striation in the area of the anterior capsule of the lens in some patients. (It may be mentioned,

incidentally, that he denied that neurodermatitis alone can produce a cataract.) This striation could be noted only with the slit lamp and with partial or complete mydriasis. This coronary radial opacification had been found hitherto mainly in glass blowers. Bücklers noted it in 72 of 100 persons whose ages ranged between 8 and 64 years. He concludes that this readily overlooked phenomenon is normal.

K. L. STOLL.

VOGT'S STRIPES (RETROIRIDIAL PIGMENT LINES IN THE ANTERIOR CAPSULE OF THE LENS) DEMONSTRATED IN TWENTY-TWO NEW CASES. V. BISCHLER, Klin. Monatsbl. f. Augenh. **103:** 517 (Oct.-Nov.) 1939.

Vogt's stripes are described and illustrated in his atlas. In 1935, Streiff published 3 further cases. Bischler adds 22 cases of Vogt's stripes, in 18 of which the patients were women. The average age was 60 years. The stripes occurred bilaterally in 19 of these 22 patients, chiefly in the nasal side of the anterior capsule. Distinct atrophy of the pupillary pigment seam was present in 13; it was limited to the area of the stripes in 4 of these and was unilateral in 2 eyes which showed numerous stripes. Isolated pigment cells, larger than those in the stripes, were noted near the anterior pole of the lens in 3 patients and fine filiform remnants of the pupillary membrane in 7; the remaining 12 patients were free from these changes. Two female patients suffered with diabetes; 2 others had syphilis of long standing. Other changes were observed, such as scintillation of the vitreous, punctate anterior seam of the lens, Krukenberg's spindle and desquamation of the anterior capsule of the lens.

Bischler supports Streiff's theory, which maintains that the pigment cells of the stripes are derived from the pigment layer of the posterior surface of the iris and that they originate after a certain age (senile pigment dispersion). This opinion would explain why the pigment cells had disappeared in 2 of the patients four years and eighteen months respectively after observation.

K. L. STOLL.

Methods of Examination

PILOT FITNESS: A SAFETY FACTOR IN AVIATION. C. E. FERREE and G. RAND, Brit. J. Ophth. **24:** 581 (Dec.) 1940.

The authors cite Major General James E. Fechet (retired) as authority for the statement that airplane crashes in more than half the cases are due to personal error or to undetermined causes. The pilot is a very important factor.

They describe an instrument for testing pilot fitness to which they have given the name multiple exposure tachistoscope. It was devised particularly for measuring the speed of adjustment of the eyes for change of distance, the speed of accommodation and the speed of adaptation and for testing ocular and general fatigue.

The instrument makes possible: (*a*) the use of a set of very sensitive tests which take into account as no other tests do both the motor and the sensory functions of the eyes in just the proportion that they occur

in the act of seeing objects in different directions and at different distances; (*b*) the testing of the dynamic speed of vision with either the oculomotor or the accommodative feature emphasized, and (*c*) the measurement of the time required to change from near to far and from far to near in combination or separately.

The following practical uses of the instrument and test procedure are discussed: (1) as a test of vocational fitness in all cases in which dynamic speed of vision is an important requirement; (2) as a test of pilot fitness for aviation; (3) as a specific performance test of fitness for night flying; (4) as a test of disturbance in fitness due to altitude; (5) as a limiting test for age as a factor in fitness; (6) as a means of measuring ocular fatigue and recovery, of testing individual susceptibility to fatigue and capacity to recover and of detecting disturbances in fitness from other causes, such as loss of sleep, worry and all mental states that distract attention, and (7) as a means of training eyes to greater oculomotor and accommodative facility.

W. ZENTMAYER.

TEST CHARTS WITH REDUCED CONTRAST BETWEEN TYPES AND BACKGROUND TO ESTABLISH VISUAL ACUITY. W. COMBERG, Klin. Monatsbl. f. Augenh. **103**: 466 (Oct.-Nov.) 1939.

Visual tests with the customary test charts bearing black letters on a glaring white background give inaccurate results because less bright illumination is frequently at the patient's disposal for distance vision. The strong contrast, on the other hand, exists only in reading. Comberg devised test charts with three grades of brightness: The first white, with the customary reflection of 75 per cent; the second light gray, with 20 per cent reflection, and the third dark gray, with 10 per cent reflection. These charts allow a more accurate graduation of the fitness of the eyes than do the customary charts. Eyes with surgical aphakia may have full vision when examined with the white chart, but examination with the light or the dark gray chart will show that the vision is insufficient for occupational requirements.

Eyes with a thin postoperative film in the pupil and eyes with fine opacities of the lens in cases of beginning cataract may show considerable visual deficiencies when examined with these charts.

K. L. STOLL.

Neurology

UNILATERAL LOSS OF VISION IN NEUROLOGICAL DISEASE. P. J. LEINFELDER, Am. J. Ophth. **22**: 1337 (Dec.) 1939.

Leinfelder reviews the symptoms of pituitary adenoma, meningioma of the sphenoid ridge, multiple sclerosis, intracranial aneurysm, suprasellar cyst, internal hydrocephalus tumors of the frontal lobe, hysteria and other infrequent causes of blindness, especially from the standpoint of unilateral loss of vision. He draws the following conclusions:

"Unilateral loss of vision should in each instance call to mind the possibility that the local condition is but a manifestation of disease of the central nervous system. In order to establish an etiologic diagnosis, it may be necessary to observe the patient repeatedly over a period of weeks. During this time, careful search should be made for new evidence

of localization or extension of the process, by frequent thorough neurologic examinations, and by attempts to elicit variations and progressions in the visual fields. Special care should be observed to demonstrate early signs of compressions of the third, fourth, fifth, and sixth nerves, for involvement of these structures is extremely suggestive of a lesion at the base of the brain. Roentgenograms may serve to locate or identify the lesion, but occasionally a diagnosis cannot be made without exploratory operation of the base of the brain."

W. S. REESE.

NEUROMYELITIS OPTICA. A. G. ATHENS, Am. J. Ophth. **22**: 1360 (Dec.) 1939.

Athens gives the following summary:

"A case of acute diffuse myelitis with sudden blindness in a 15-year-old boy is reported. The fields showed large central scotoma and loss of color sense for red and green. There was deep orbital pain, particularly on rotating the eyes. Three weeks after the onset of blindness there was rapid development of myelitic symptoms beginning with weakness of the legs, uncertain gait, and soreness in the lower back. Retention of urine began early, and later there was constipation and incontinence of stools. The cord symptoms spread upward. The patient developed extreme vertigo and loss of sense of position of the extremities. A high-grade cardiac arrythmia developed and was misinterpreted as indicating myocarditis. The tendon reflexes were hyperactive. There were 180 cells in the spinal fluid and an increase in the blood leucocytes. Recovery was rapid and nearly complete.

"While showing many of the symptoms of multiple sclerosis, the high degree of bilateral visual loss, the age of the patient, and no sign of relapse after several months would seem to distinguish it as a separate disease. The cases that have come to autopsy have furnished considerable pathologic evidence that would tend to further differentiate this disease from multiple sclerosis."

W. S. REESE.

LESIONS OF THE FUNDUS ASSOCIATED WITH BRAIN HEMORRHAGE. L. L. TUREEN, Arch. Neurol. & Psychiat. **42**: 664 (Oct.) 1939.

Twenty-three cases of cerebral hemorrhage with papillary swelling and retinal bleeding are reviewed in this report.

Swelling of the optic disk was found associated most often with intraventricular hemorrhage, which was not accompanied with a subarachnoid or a pontile hemorrhage. Retinal hemorrhages were not found to be characteristically associated with retinal arteriosclerosis but occurred in the course of subarachnoid and pontile hemorrhage. The appearance of papilledema and retinal hemorrhages in cases of cerebral hemorrhage leads on occasion to difficulties in differentiation of such hemorrhage from tumor of the brain.

Bleeding into the subarachnoid space of the optic nerve sheath, a common accompaniment of hemorrhage into the meninges of the brain, may produce mechanical compression of the central retinal vein as it emerges from the optic sheaths, rapidly producing the effects of stasis. This effect would be exerted in addition to the elevation of intervaginal

pressure accompanying intracranial rise. Probably this mechanism explains the frequency of retinal hemorrhages in the cases of subarachnoid hemorrhage under discussion.

R. IRVINE.

HISTOPATHOGENESIS OF CEREBRAL ABSCESS. F. A. CARMICHAEL JR., J. W. KERNOHAN and A. W. ADSON, Arch. Neurol. & Psychiat. **42:** 1001 (Dec.) 1939.

This article reviews the etiologic aspects of cerebral abscess and presents a detailed study of the evolution of the lesion, based on the gross and microscopic study of 60 brains. Of chronic infections of the head and face particularly predisposing to abscess of the brain, infections in and about the orbit are said most consistently to produce cerebral abscess. In the authors' series there were 3 cases of such infection.

R. IRVINE.

SPONTANEOUS HEMORRHAGE INTO OCULOMOTOR NERVE WITH RUPTURE OF NERVE AND FATAL SUBARACHNOID HEMORRHAGE. A. PLAUT and M. DREYFUSS, Arch. Neurol. & Psychiat. **43:** 564 (March) 1940.

A case is presented of spontaneous hemorrhage into the intracranial portion of the oculomotor nerve, with subsequent self amputation of the nerve and resulting subarachnoid hemorrhage.

No other report of such self amputation due to hemorrhage could be found.

The literature contains the reports of 1 other case of spontaneous hemorrhage into the third nerve and of 2 such occurrences associated with tuberculous meningitis.

R. IRVINE.

Ocular Muscles

CONVERGENCE WEAKNESS. O. G. MORGAN, Brit. J. Ophth. **24:** 564 (Nov.) 1940.

Morgan has found "that quite a number of people seemed to have no convergence at all, and yet had no symptoms of eye strain with near work or reading." Persons with convergence weakness may, however, have severe clinical symptoms. Several illustrative case reports are given. It is certainly a central failure, because the training in some cases is rapid, depending on how quickly the patient understands what is required of him. It seems to be a subconscious suppression of an associated movement.

W. ZENTMAYER.

Operations

POLYVIOL IMPLANTS FOR PLASTIC FORMATION OF A STUMP AFTER ENUCLEATION OF THE EYEBALL. R. THIEL, Klin. Monatsbl. f. Augenh. **103:** 530 (Oct.-Nov.) 1939.

Thiel reports on his results with implants made of a new composition called polyviol. It is a preparation consisting of a polyvin alcohol and water, with or without addition of substances exerting a specific action on the polyvinyl alcohol, e. g., congo red. The resulting substance remains

firm under body temperature but becomes liquid under higher temperatures. The implants are globular, with a flat, rounded-off surface which is turned toward the rear of the orbit. Insertion into Tenon's capsule follows enucleation, and a tobacco pouch suture of catgut is used to close the wound of the conjunctiva. Thiel states that the cosmetic results are satisfactory and that the implants withstand chemical influences; they are tolerated well in the orbit.

K. L. STOLL.

Refraction and Accommodation

VITAMIN-D COMPLEX IN PROGRESSIVE MYOPIA. A. A. KNAPP, Am. J. Ophth. **22:** 1329 (Dec.) 1939.

Knapp studied 53 patients over periods ranging from five to twenty-eight months, all of whom were chosen because it was believed that their myopia would progress. Their ages ranged from 3 to 20 years and their myopia from —0.25 to —0.41 D. The following conclusions are reached:

"From this study, it appears that a disturbance in the vitamin-D-calcium-phosphorus metabolism is concerned in the etiology of myopia. In the presence of a calcium imbalance, there may be a weakening of the fibrous tunic, which may give rise to myopia. Once a condition of progressive myopia has been established, treatment with the vitamin-D complex is indicated. The myopic eyes that respond to this therapy may undergo an actual shrinkage of the globe.

"For the prevention of the onset of myopia, the vitamin-D complex probably has another field of usefulness. Given a patient showing a diminishing degree of hyperopia, and one who is approaching the axial myopia side, it would be well to fortify his diet with vitamin D and calcium."

W. S. REESE.

Retina and Optic Nerve

VASCULAR BED OF THE RETINA IN MENTAL DISEASE. J. M. COTTON, N. D. C. LEWIS and A. W. EGENHOFER, Arch. Neurol. & Psychiat. **43:** 891 (May) 1940.

The cross-sectional area of the vascular bed of the retina has been measured in a group of psychiatric patients classified as having either schizophrenia or manic-depressive psychosis. It is believed that these measurements are an index of the developmental status of the general vascular constitution of the patient.

The fundus was studied with the Gullstrand ophthalmoscope, and the caliber of vessels was determined after correction for the magnification factor dependent on the refraction.

R. IRVINE.

RETINITIS PIGMENTOSA AND ASSOCIATED NEUROPSYCHIATRIC CHANGES. S. B. WORTIS and D. SHASKAN, J. A. M. A. **114:** 1991 (May 18) 1940.

Forty-one patients came from thirty-two families and thirty-three sibships; eighteen of these families had more than one member affected with this ocular difficulty. Consanguinity was present in two families

(6 per cent), an incidence obviously greater than that which occurs in the general population. The patients' ages ranged from 11 to 69 years, the majority being over 30.

The authors give the following summary:

"In forty-one cases of retinitis pigmentosa:

"1. Three fifths of the patients are males.

"2. In most families more than one member is affected.

"3. Two fifths of the patients are deaf.

"4. Other somatic and psychologic defects are commonly found.

"5. In spite of their visual disturbances these patients make a happy social adjustment, but if deafness precedes their blindness they may have mild paranoid changes.

"6. There is biologic evidence of a general body metabolic disturbance in patients suffering with retinitis pigmentosa."

The article is illustrated.

J. A. M. A.

Trachoma

A NOTE ON THE IMMUNOLOGY OF TRACHOMA. L. A. JULIANELLE, Am. J. Ophth. **22**: 1326 (Dec.) 1939.

After experiments, Julianelle draws the following conclusion:

"Artificial immunization of rabbits and susceptible monkeys, accomplished by repeated intravenous injections of conjunctival scrapings from the eyes of patients with clinically active trachoma, does not stimulate antibodies capable of neutralizing the virus of this infection."

W. S. REESE.

Tumors

MALIGNANT MELANOMA OF THE CHOROID AND VON RECKLINGHAUSEN'S DISEASE. S. GARTNER, Am. J. Ophth. **23**: 73 (Jan.) 1940.

Gartner gives the following summary of these rarely associated diseases:

"The occurrence of malignant melanoma of the choroid and von Recklinghausen's disease in the same individual is reported.

"Evidence is submitted for grouping these diseases as neurogenic tumors in a related etiology.

"The following are considered to be features of their association: 1. Melanin is found in both. 2. Dopa reaction is positive for both. 3. Both originate from neuroectoderm. Malignant melanoma of the choroid has been traced anatomically from the ciliary nerves. Neurofibromas are intimately associated with the nerves from which they arise. Both have been traced from the Schwann layer of syncitial cells surrounding the nerves. 4. Neurofibromas have been found in the eye, mainly in the uveal tract. They are located in the same regions as malignant melanomas. 5. Both show a tendency to form structures resembling Wagner-Meissner tactile corpuscles. 6. In von Recklinghausen's disease, 13 per cent of the cases undergo malignant degeneration. It has

been suggested that some cases of malignant melanoma develop from neurofibroma. It has also been suggested that some cases diagnosed as malignant melanoma, particularly the leukosarcoma, are really neurofibroma. 7. Three previous cases have been reported in the literature, showing the association of malignant melanoma and von Recklinghausen's disease in the same individual."

W. S. REESE.

BOECK'S SARCOIDOSIS OF THE LACRYMAL GLANDS. H. B. STALLARD, Brit. J. Ophth. **24**: 451 (Sept.) 1940.

A married woman 45 years old was seen on July 18, 1939. There had been an increasing swelling of the upper outer angle of the right orbit for six months. The mass occupied the position of the lacrimal gland; it was slightly nodular and of firm elastic consistence. It was attached to the orbital tissues but not to the skin or bone. There were no cutaneous lesions characteristic of Boeck's sarcoidosis. In 1932 and 1933 there were lassitude, night sweats and swelling behind the right ear and on both sides of the neck. There were enlarged lymph nodes behind the right auricle, in the neck and in the axillas. The spleen was enlarged. Roentgenograms showed enlarged hilar shadows on both sides and posterior mediastinal opacities. The blood picture was not significant. Biopsy of a lymph node showed evidence of chronic inflammation but not of lymphadenoma.

Roentgen ray treatment was given, and subsequently the orbital growth was removed. The author makes the following commentary:

"From the clinical features in 1932 and 1933, and the histological appearance of the excised lymph node, it was evident that this patient was suffering from a disorder of the reticulo-endothelial system. Neither the microscopic examination at this time nor the subsequent clinical history suggested lymphadenoma.

"Her symptoms and signs subsided after about 18 months, and she remained well until recurrence in the right lacrymal gland in 1939. The histological features of the excised lacrymal gland swelling resembled those seen in Boeck's sarcoidosis. In this disorder, all the tissues of the reticulo-endothelial system are not necessarily involved and although lymphadenopathy is evident in all cases at some stage in the disease, one group of nodes may be affected at one time and another later. In this case lymphadenopathy, splenomegaly, mediastinal changes and later involvement of the right lacrymal gland were the chief clinical features."

One illustration accompanies the article.

W. ZENTMAYER.

Society Transactions

EDITED BY W. L. BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

FRANCIS HEED ADLER, M.D., *Chairman*

WARREN S. REESE, M.D., *Clerk*

April 17, 1941

Is Enucleation Indicated in Cases of Early Intraocular Malignant Melanoma? DR. L. LEHRFELD.

Two cases of intraocular melanosarcoma were reported, in which the patients were 49 years of age and had had symptoms since the onset of the disease.

In the first case an early clinical diagnosis was made, the tumor having been precipitated by an injury to the eye six months previously. The eye was removed, after which radium was applied to the socket. The patient died less than eight years later from metastases to the lung and vertebrae. The tumor was classified pathologically as spindle cell sarcoma of type B.

In the second case a diagnosis was made of secondary glaucoma, and an intraocular tumor was suspected. The patient refused to give permission for enucleation until eleven years later, when proptosis occurred. The eyeball was removed together with a large tumor which was adherent to the posterior segment. The patient died as the result of an automobile accident, at which time he suffered a fractured skull. At autopsy a tumor was observed in the region of the chiasm, and it extended to the floor of the third ventricle. There was no other evidence of metastasis.

The two cases were reported to show that early enucleation in itself is not absolute assurance of longevity.

In the second case, in which the tumor was diagnosed as epithelioid in type or as a highly malignant form of melanoma, metastasis did not actually result, but the tumor extended through the eyeball to the optic chiasm and to the brain substance. Despite the highly malignant character of the tumor and despite the patient's refusal to submit to enucleation, he lived longer than the patient whose eye was removed during the early stages of tumor formation.

Because malignant melanomas of the eye originate from neuroectodermal tissue which forms from the cells of Schwann of the sheaths of the ciliary nerves, the theory is propounded that denervation of the eyeball should deprive the tumor of the nerves from which it grows and thereby retard its growth. The intraorbital injection of alcohol is proposed to accomplish denervation in a like manner, as neurosurgeons use alcohol to alleviate pain. The suggestion is made that application of this theory will result in spontaneous necrosis of tumor cells or at least render them more sensitive to treatment by roentgen rays and radium.

DISCUSSION

Dr. W. E. Fry had an opportunity to see the two sections from the cases which Dr. Lehrfeld reported. In his opinion it was difficult to make a definite diagnosis of malignant melanoma. He stated that the 2 cases illustrated very well the importance of the work that is being done at the Army Medical Museum in Washington, D. C., under the direction of Lieutenant Colonel Ash and Colonel Callander. They have followed cases of this type throughout the country, and they realize that no one physician can follow enough of these cases to draw accurate conclusions because of the rarity of this disease. The classification, which Colonel Callander originated and which is followed at the Museum, and the new silver staining method, which is used there to designate accurately the grade of malignant melanoma of the eye, give a fair clue statistically regarding the longevity of a patient after the eye has been enucleated. In a given case the classification may not be absolutely correct, and they realize this, but at present it is the best known one to follow.

It is true that many pathologists consider melanoma to be ectodermal in origin. To Dr. Fry's knowledge, the opinion that intraocular malignant melanoma of the eye is of ectodermal origin is based on the report of 1 case, in which serial sections were made and staining was done according to Masson's trichrome method. Dr. Frey stated the belief that opinions should be reserved regarding the origin of malignant melanomas of the eye until more research has been carried out. In Dr. Fry's opinion, an eye should be enucleated as soon as a diagnosis of intraocular melanoma has been substantiated.

Dr. F. H. Adler asked Dr. Lehrfeld if he meant to intimate that metastasis is hastened by enucleating an eye which contains a malignant melanoma. Dr. Adler stated that he did not believe this to be so. According to statistics gathered by von Hippel, deaths from metastasis are about in the same ratio in cases in which enucleation has been carried out during the early stages of the disease as in cases in which it has been carried out during the late stages of the disease. The term early is relative, and such a designation really implies that this diagnosis is not made early enough. A lesion which is classified as early may still be capable of causing metastasis, in which case the diagnosis has been made too late. The best way to denervate a tumor of this kind is to enucleate the eye.

Dr. Lehrfeld stated that von Hippel reported a mortality of 62 per cent five years after enucleation and 30 per cent ten years after enucleation, which totals 92 per cent, in cases of melanosarcoma in which enucleation had been performed and in which death from metastases occurred within ten years after removal of the involved eye. There are no data comparable to these in cases in which enucleation was not performed. It must, therefore, be assumed that enucleation itself must have some bearing on metastasis and mortality.

Dr. Adler inquired about early enucleation to avoid metastasis. The 2 cases just reported prove that early diagnosis and early enucleation did not prevent death from metastasis. From a practical standpoint, early diagnosis is not often possible. It is estimated that in 40 per cent of the cases of intraocular malignant melanoma the original diagnosis is made by the pathologist who makes the sections from the enucleated eye.

There is no set rule by which a positive clinical diagnosis can be made early, particularly a diagnosis which will help to determine the grade of malignancy.

Should early clinical diagnosis be possible, there is no definite proof that enucleation will save or extend life. Possibly the best treatment in the future will be denervation followed later by enucleation. Dr. Lehrfeld was not sure of this. Only further experimentation and trial will reveal further information.

Recently Dr. Lehrfeld conferred with Dr. Widmann, chief of the cancer clinic of the Philadelphia General Hospital, concerning his proposed plans. Dr. Widmann stated that a method had been advocated which consisted of injection of water into the body of a tumor to make it more sensitive to radiotherapy. He felt that injection of alcohol might be an additional advance in making melanosarcoma sensitive to radium and roentgen rays.

Dr. Lehrfeld stated that enucleation in cases of early intraocular melanoma is still in the experimental stages but that further investigation should determine the value of denervation by retrobulbar injection of alcohol.

Operative Treatment of Early Strabismus. DR. G. GIBSON.

Dr. Gibson reported a group of cases of concomitant convergent strabismus present in patients between the ages of 3 and 5 years, in which there was no improvement from glasses in from three to six months. Marginal myectomy had been performed, and parallelism was reestablished. Within one to two months fusion developed without the aid of training exercises. There was no significant sequela of the strabismus. In view of these satisfactory results, it was suggested that surgical intervention should be done early in the course of strabismus, in order to permit binocular vision to develop before it is too late. Because of the possibility of postoperative divergence, attention was called to the fact that for early strabismus less surgical correction is indicated than for long-standing strabismus of a similar degree.

DISCUSSION

Dr. Ellis asked if Dr. Gibson had operated on the two eyes of a patient at the same time, performing bilateral recessions.

Dr. Gibson answered that he had operated on two eyes at the same time in a case in which the procedure was indicated.

Penetration of Sulfanilamide and Its Derivatives into the Aqueous Humor. DR. H. G. SCHEIE and DR. B. F. SOUDERS.

This paper was published in full in the June issue of the ARCHIVES (**25:** 1025, 1941).

DISCUSSION

Dr. Gibson asked Dr. Scheie if he had had any clinical experience that would correlate the investigations made of cats' eyes to prove or disprove this assumption.

Dr. Scheie answered that he had not mentioned any of his clinical experiences because the cases in which he had used sulfathiazole were

few—3 to be exact. In a case of a penetrating wound of the eye the sulfathiazole seemed to have no effect. In a case of postoperative cataract the drug did not alter the course of the infection. In a case of ring abscess of the cornea, in which it was not fair to judge the effectiveness of the drug, the results were unfavorable.

Ocular Conditions Associated with Rheumatoid Diseases. DR. M. L. KAUFFMAN.

Dr. Kauffman stated that the patients studied were from the service of Dr. Ralph Pemberton at the Abington Memorial Hospital. Twenty-nine of 117 outpatients and 91 of 96 ward patients were examined. Certain ocular conditions are more prevalent in patients suffering from rheumatoid disease than in other persons in the same age group.

The conditions observed were tabulated according to the ages of the patients, by decades. Uveitis, either chronic or recurring, was the commonest condition. Episcleritis and conjunctivitis were next in prevalence. Conjunctivitis was apt to be subchronic and the secretions scant, the symptoms being more marked than the external appearance would indicate. There was suggestive evidence that sclerosis of the retinal vessels, spastic arterioles and changes in the lens occurred at a somewhat earlier age in patients with rheumatoid disease than in patients in general. Xanthelasma was noted 3 times in the entire group. Changes in the nerve head, characterized by hyperemia and pallor, were noted several times. Atrophy of the optic nerve was present in at least 2 patients. Partial pallor of the disk was seen frequently without other ophthalmologic evidence of atrophy of the optic nerve. This may have been due to changes in the finer vessels.

DISCUSSION

Dr. F. H. Adler stated that he was surprised to learn that there were not more ocular diseases present in a group of patients who were hospitalized for a serious illness of this type. He spoke of subacute recurring iritis and scleritis, which are due to rheumatoid disease. Furthermore, it is generally known that patients suffering from rheumatoid disease do not make satisfactory progress after intraocular surgical intervention, particularly cataract extraction.

Pathologic Picture of the Retinal Blood Vessels in Hypertension, Arteriosclerosis and Diabetes Mellitus. DR. P. J. KENNEDY.

Dr. Kennedy reported that the histologic changes of diseased retinal blood vessels are similar to those of blood vessels elsewhere in the body. The outstanding fundus picture produced by retinal disease is that of retinal hemorrhages and exudates. These manifestations indicate the severity of the disease and are not seen in the early stages. The hemorrhages result from diseased walls of blood vessels, increased intravascular pressure or both. Exudates may be the result of previous hemorrhages or of varying degrees of tissue anoxemia. Anoxemia causes cellular degeneration and, if severe, destruction of cells.

The size, shape and definition of retinal hemorrhages are indicative of their location in various layers of the retina. The size, number and

distribution of exudates aid in determining whether the retinal damage is being caused mainly by hemorrhage or by slow destruction of tissue as a result of decreased blood supply.

The type of retinitis present is determined by the associated clinical picture. Hemorrhagic, exudative, hypertensive, arteriosclerotic, nephritic and diabetic chorioretinitis, optic neuritis and occasionally other diseases of the retina are all characterized by vascular pathologic changes, hemorrhages and exudates. Histologically, the vascular picture in all of these conditions is similar, but the presence of diabetes, hypertension or renal disease determines how the particular type of retinitis that is seen through the ophthalmoscope should be classified.

Lantern slides showing photomicrographs of diseased eyes in which were present the clinical conditions mentioned were shown, and the similarity of the vascular changes associated with these diseases was pointed out.

The amount and rapidity of retinal destruction in any of these conditions is directly proportional to the changes in the size of vascular lumens, abnormal vascular permeability and the intravascular blood pressure.

DISCUSSION

Dr. T. Cowan cited Dr. Kennedy as having stated that there are similarities in the vascular pictures of these various conditions. Dr. Cowan affirmed, on the other hand, that retinitis due to arteriosclerosis and retinitis due to diabetes are dissimilar clinically. He stated the belief that he could tell the difference between the two and that other ophthalmologists are likewise able to do so. He asked what the differences are pathologically and expressed the opinion that that question has never been answered, which is one failing in pathology of the retina. Dr. Cowan stated that he hoped either Dr. Kennedy or some other pathologist at some future date would be able to reveal the differences as well as the similarities.

Book Reviews

Manual of the Diseases of the Eye. By Charles H. May, M.D. Seventeenth edition. Price, $4.00. Pp. 519, with 387 illustrations, including 32 plates with 93 colored figures. Baltimore: William Wood & Company, 1941.

After two years this popular manual now appears in a new edition. It has been carefully revised, some of the text has been rewritten and new illustrations, both in color and in black and white, have been added without increasing the size of the book. Of particular importance is the appendix giving the ocular requirements for admission to the Army, Navy and Marine and Air Corps of the United States.

The author and his capable assistant, Dr. Charles A. Perera, have admirably succeeded in bringing the contents of this book up to date, thus insuring the continuation of its just popularity.

ARNOLD KNAPP, M.D.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Consolacao, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. A. J. Ballantyne, 11 Sandyford Pl., Glasgow, C. 3, Scotland.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Lawrence T. Post, 508 N. Grand Blvd., St. Louis, Mo.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Atlantic City.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank R. Spencer, Physicians' Bldg., Boulder, Colo.
President-Elect: Dr. Ralph I. Lloyd, 14–8th Ave., Brooklyn.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Chicago. Time: Oct. 19-24, 1941.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Allen Greenwood, 82 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Vaillancourt, 46 St. Louis St., Quebec.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. V. May, 1703 Main St., Marinette.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Marinette. Time: November 1941.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. E. Rideout, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Franklin P. Maury, Professional Bldg., Tucson, Ariz.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. J. K. Heckert, 103 N. Washington St., Lansing.
Secretary-Treasurer: Dr. W. D. Irwin, 710 Hanselman Bldg., Kalamazoo.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. Edward N. DeWitt, 836 Myrtle Ave., Bridgeport.
Secretary-Treasurer: Dr. Henry L. Birge, 179 Allyn St., Hartford.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. A. L. Hammerel, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. A. E. Spear, Dickinson.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. Roderick Macdonald, Rock Hill.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.
Place: Columbia Hotel, Columbia. Time: November 1941.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
Place: San Antonio. Time: December 1941.

Utah Ophthalmological Society

President: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 628 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. George G. Hawkins, Newport News.
Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert D. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Harold Mulligan, 1680 N. Vine St., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Leonard C. Whiting, 121 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.
Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. James W. Smith, 1016–5th Ave., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward A. Weisser, 119–5th Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. William M. James, 508 N. Grand Blvd., St. Louis.
Secretary: Dr. H. Rommel Hildreth, 823 Metropolitan Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. John D. Skow, 2001 Collingwood Blvd., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Sterling Bockoven, 1752 Massachusetts Ave. N.W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.